"A Study to Evaluate the Intraoperative Imprint Smears of Breast Tumours with Histologic Correlation''

Dissertation submitted

To

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY, CHENNAI

With partial fulfillment of the regulations for the award of the degree of

M.S (General Surgery)

Branch-I

Government Kilpauk Medical College

Chennai- April -2016

CERTIFICATE

This is to certify that this dissertation is the bonafide work of

DR J.JESLIN

on

“A study to evaluate the intraoperative imprint smears of breast tumours with histologic correlation’’

During her course in M.S. General Surgery from JANUARY 2015 toJUNE 2015 at Government Kilpauk Medical College, Chennai-10.

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This is to certify that the dissertation titled **"A study to evaluate the intraoperative imprint smears of breast tumours with histologic correlation''**is a bonafide research work done by **Dr.J.JESLIN**, post graduate in M.S. General Surgery, Kilpauk Medical College, Chennai-10 under my direct guidance and supervision in my satisfaction, in partial fulfillment of the requirements for the degree of **M.S. General Surgery**.

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled "**A study to evaluate the intraoperative imprint smears of breast tumours with histologic correlation''** is a bonafide and genuine research work carried out by me under the guidance of Prof. Dr.P.N.Shanmugasundaram M.S, HOD, Department of General Surgery, Kilpauk Medical College, Chennai-10.

This dissertation is submitted to **THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY CHENNAI** in partial fulfillment of the degree of M.S. General Surgery examination to be held in **April 2016**.

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Place: Chennai

Date: **Dr. J. JESLIN**

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID.No.17/11/2014
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A study to evaluate the accuracy of intra operative imprint smear in breast tumours with histological correlation at Govt. Kilpauk Medical College Hospital"- For Project Work submitted by Dr.J.Jeslin, IInd Year M.S.Surgery PG, Department of General surgery, Govt. Kilpauk Medical College and Hospital, Chennai-10.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

20/1/15

CHAIRMAN,
Ethical Committee
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19/1/2015

A STUDY TO EVALUATE THE INTRAOPERATIVE IMPRINT SMEARS OF BREAST TUMOURS WITH HISTOLOGIC CORRELATION

TABLE OF CONTENTS

INTRODUCTION

INTRODUCTION

India is experiencing an unprecedented rise in the incidence of breast cancer as all other countries. Since there is no preventive measures for breast cancer, it is necessary to detect it early and treat adequately to achieve a longer survival. Fine needle aspiration cytology is a widely accepted diagnostic tool. But it has limitations in terms of sensitivity, specificity and diagnostic accuracy. The noble quality of FNAC depends on the proficiency of the aspirator, and its analysis is determined by the experience of the pathologist.

Many times FNAC diagnosis is suspicious but not confirmatory. And also risk of over treatment that is mastectomy could be done on the ground of false positive diagnosis. Hence the need for intra-operative confirmation of the condition of the tumour to make a therapeutic decision, led to the development frozen section technique.

But it requires specialized equipment, freezing of tissues and serial sectioning. Imprint smear cytology is the substitute to frozen section. And it is taken from the tumours and stained with eosin and haematoxyllin. It does not require specialized equipment. Imprint cytology has become important tool for diagnosis of various lesions as it is rapid, inexpensive and less time consuming.

Therefore, this work is done to assess the accuracy of intra operative imprint smear.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

“Black bile, karkinos, Nun’s disease and God’s punishment” are various names for breast cancer. In India it is the first most common cancer in urban women and second most common in rural women after cancer cervix. The overall five yearr survival rate has been increasing and it is 89% but in India it is 59%.

Women under age 40 are much less likely to develop breast cancer. But the five-year relative survival rate is lower than it is for women over 40. Younger women are more likely to be diagnosed with aggressive types of breast cancer that tend to spread faster and are more likely to recur.

With the goal of diagnosing the disease at an earlier stage various diagnostic methods have been developed.

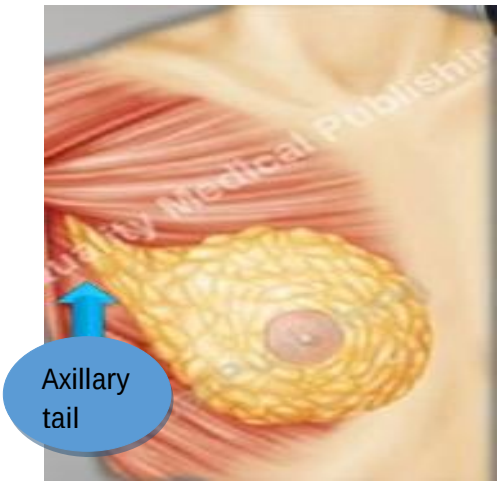
Owing to early diagnosis and improved treatment modalities, the mortality due to breast cancer has significantly reduced.

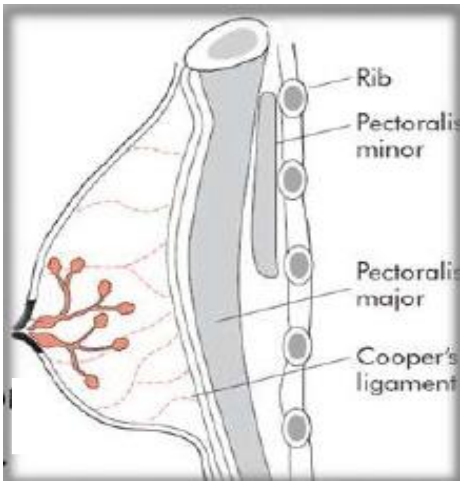
SURGICAL ANATOMY

Breast or mammary gland is a modified sweat gland. It lies in the superficial fascia.

The mature female breast extends from 2nd to 6th rib vertically and from lateral border of sternum to the anterior axillary fold transversely. A thin layer of breast tissue extends above the clavicle and to the 7th rib below .The aim of mastectomy is to remove whole of the breast tissue and hence this has to be remembered.

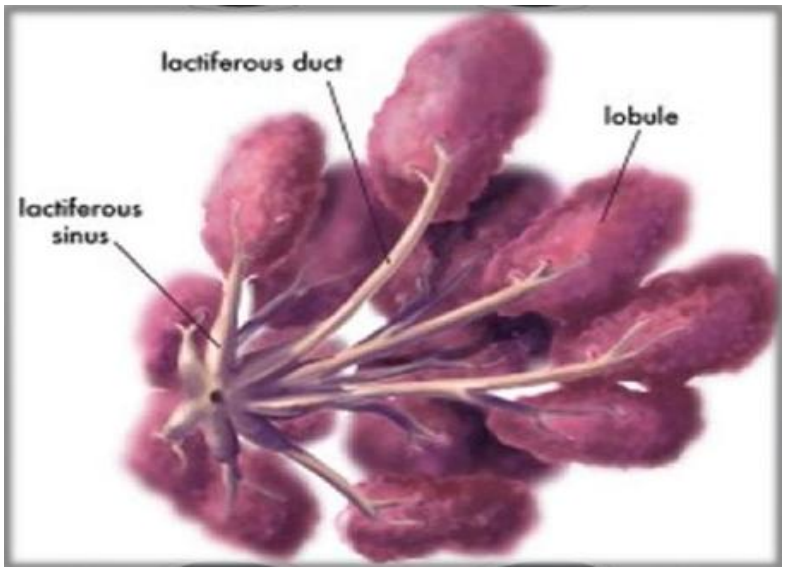
The axillary tail of Spence extends from the lateral border of breast piercing the deep fascia into anterior axillary fold and if well-developed it is mistaken for lymph node mass or lipoma.





Cooper's suspensory ligaments are fibrous strands of connective tissue that traverse the breast from the pectoral fascia and insert into the dermis perpendicularly to provide structural support. They are responsible for dimpling of skin overlying atumour.

The posterior surface of breast lies over pectoral fascia covering pectoralis major,serratus anterior and upper portion of rectus sheath. The loose areolar tissue (retromammary space) lies between breast and pectoralis fascia.

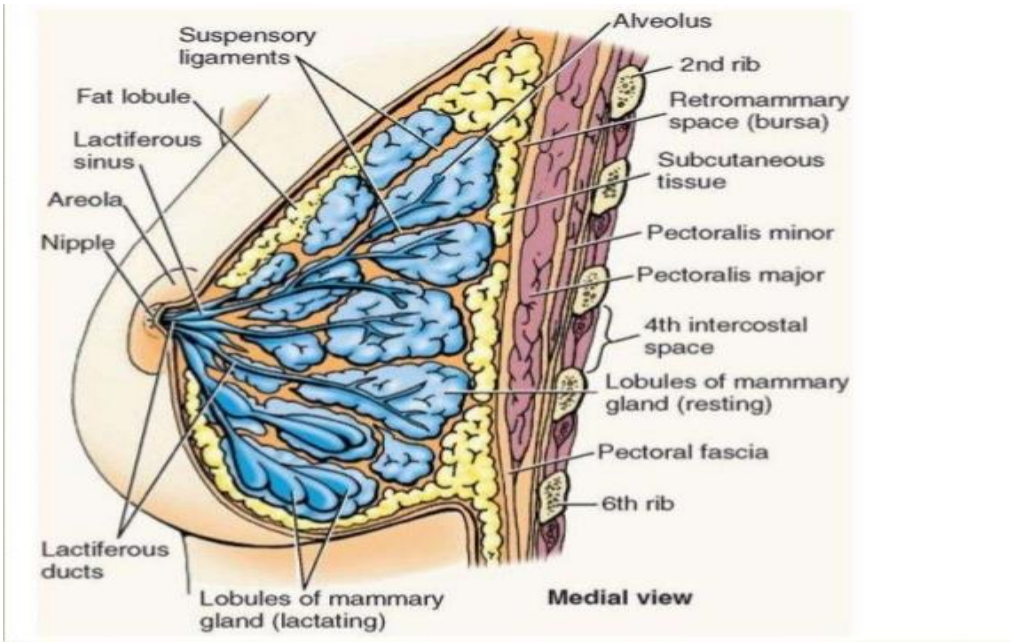


The breast parenchyma is made up of glandular tissues. The gland contains 15 to 20 lobes composed of numerous lobules which vary from 10 to 100 .each lobe is drained by lactiferous ducts which converge towards the nipple. Near its termination it is provided with a terminal dilatation called lactiferous sinus or ampulla,which is a reservoir for milk or any discharge.Both the alveoli and the ducts are lined bymyoepithelial cells which facilitates milk secretion.

The stroma forms the supporting tissue of the breast,it is partly fibrous and partly fatty.

The nipple is a conical projection just below thecentre of the breast. It is pierced by lactiferous ducts at its apex. It contains both longitudinal and circular muscle fibres that keeps the nipple erect and stiff. It has rich sensory nerve endings.

The areola is a circularpigmented area at the base of the nipple. It is rich in sweat and sebaceous glands, which becomes enlarged during pregnancy and lactation to form Montgomery tubercles,for lubrication.

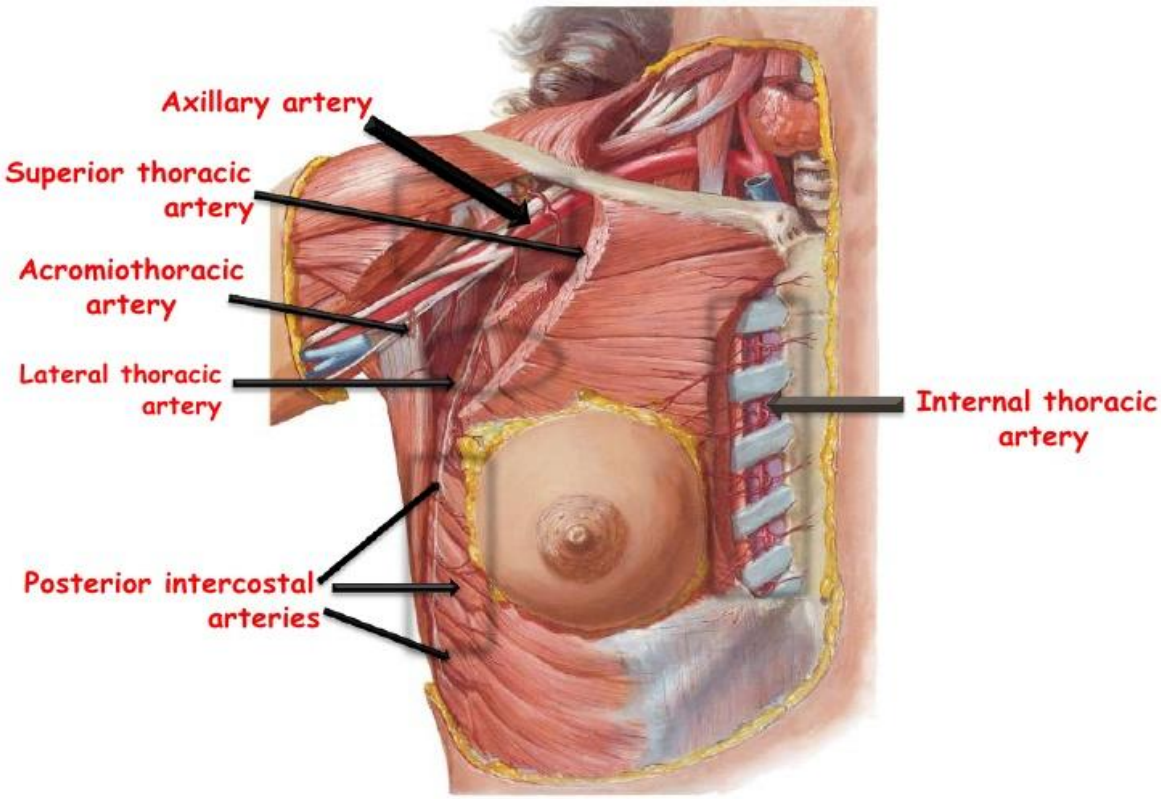


BLOOD SUPPLY:

It is extremely vascular and is supplied by

- Perforating branches of Internal thoracic artery,
- Lateral br of posterior intercostal arteries,
- Lateral thoracic ,superior thoracic and pectoral br of acromiothoracic-branches of axillary artery .

The posterior surface breast tissue is relatively avascular.



VENOUS DRAINAGE:

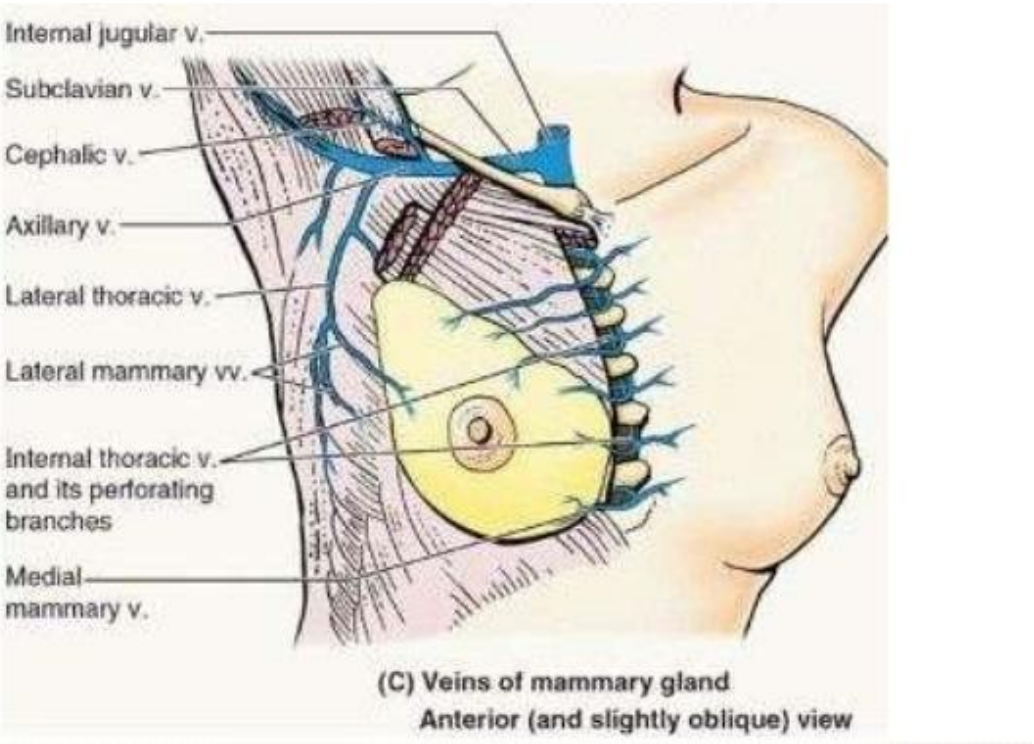
The veins follow the arteries.

Veins converge around the nipple to form anastomotic circle

They form:

Superficial veins: they drain into internal thoracic vein and

Deep veins:they drain into internal thoracic vein, axillary vein, and posterior intercostal vein.

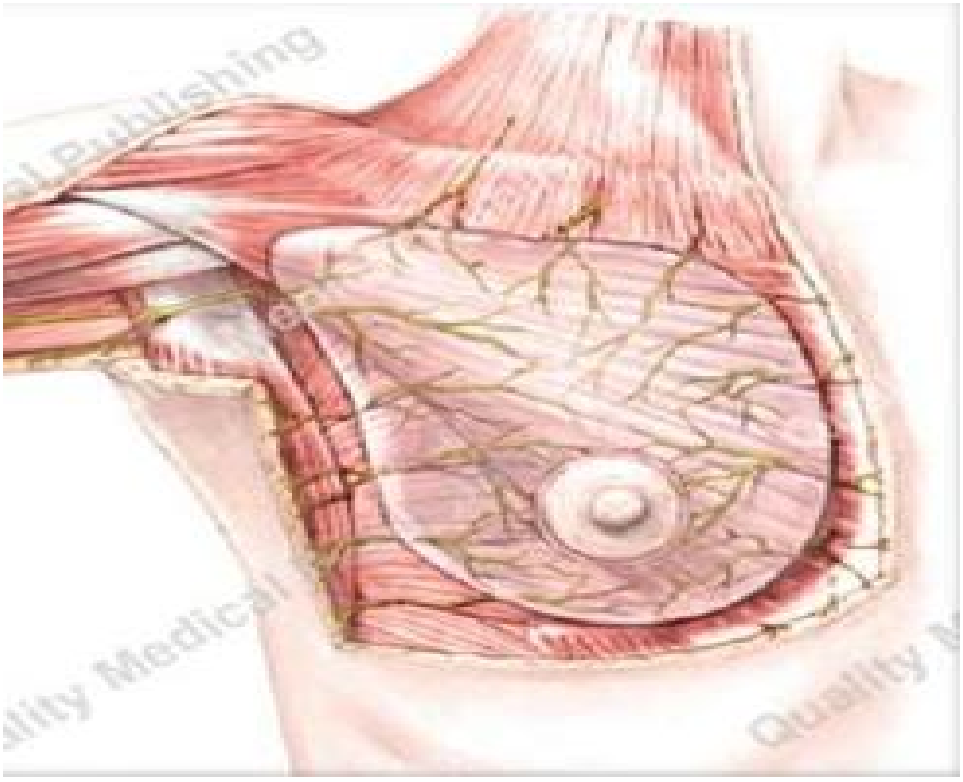


(C) Veins of mammary gland
Anterior (and slightly oblique) view

NERVE SUPPLY:

4^{th} to 6^{th}intercostals nerves through anterior and lateral cutaneous branches

Milk secretion is by the action of prolactin, not by nerves.



LYMPHATICS:

Carcinoma of breast predominantly spread through lymphatics to the regional lymph nodes. About >75% of lymph from the breast drains into the axillary nodes and they are;

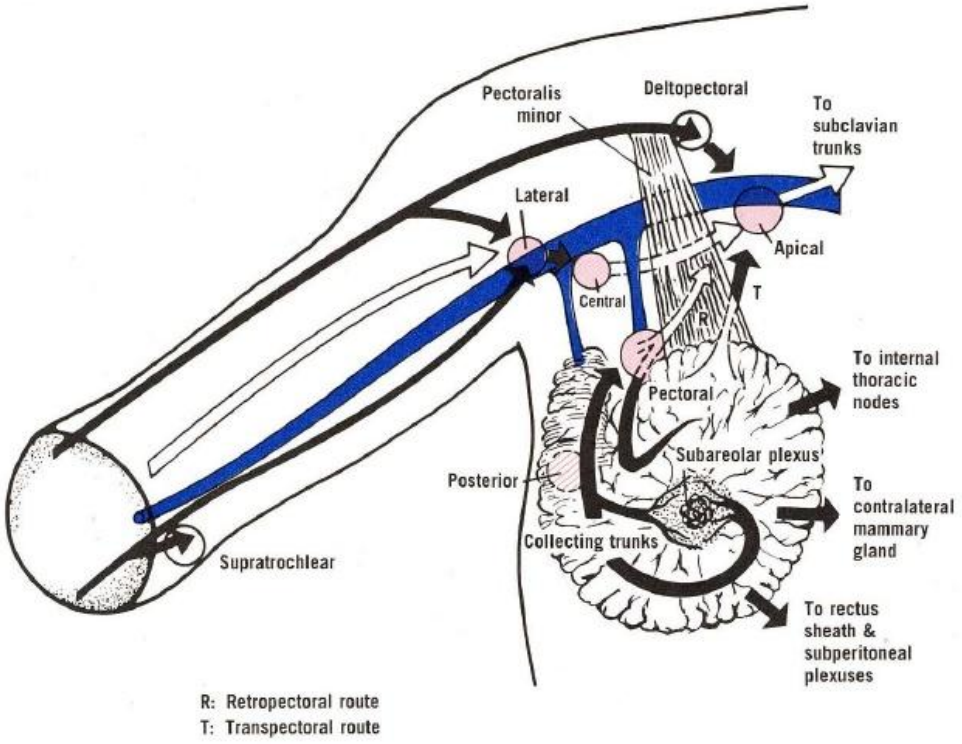
AXILLARY:

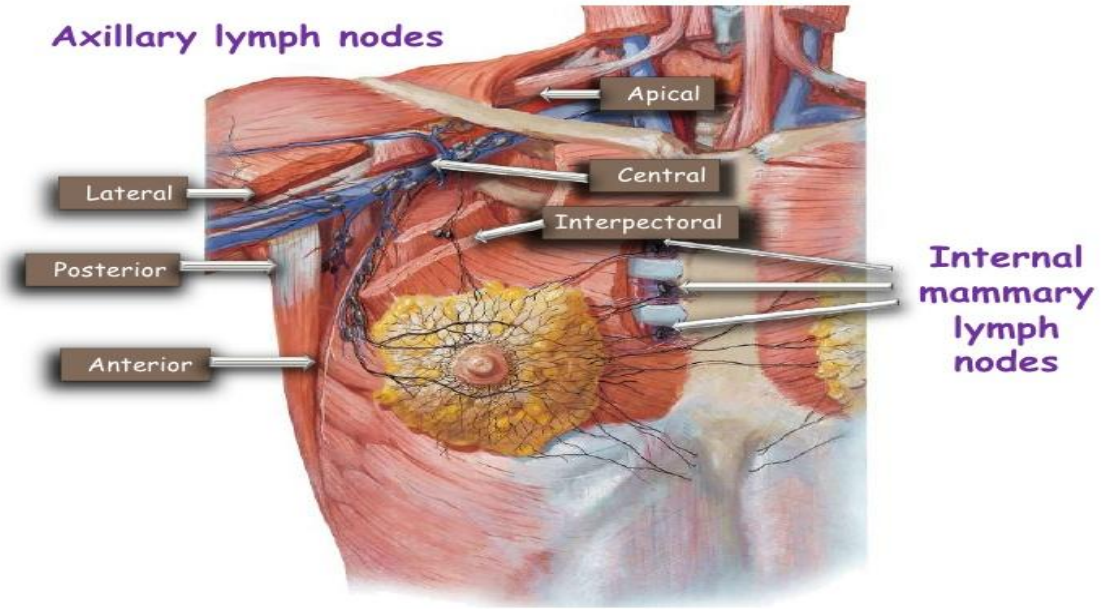
- Anterior or pectoral group- along lateral thoracic vessels
- Posterior or scapulargroup-along subscapular vessels
- Lateral or deltoid group-along axillary vein
- Central group-embedded in the fat of axilla
- Apical or subclavicular group-superior to the pectoralis minor tendon,receives from all other groups of axillary nodes. Finally drains into supraclavicular nodes
- Interpectoral or rotter's node - between pectoralis major and minor muscles

Internal mammary or parasternal nodesalong internal mammary vessels (10%)

Others (5%):

- Supraclavicular
- Cephalic / deltopectoral
- Posterior intercostals
- Subdiaphragmatic
- Subperitoneal


Pectoralis minor
Deltopectoral
To subclavian trunks
Lateral
Apical
Central
T
R
To internal thoracic nodes
Pectoral
Subareolar plexus
Posterior
To contralateral mammary gland
Collecting trunks
Supratrochlear
To rectus sheath & subperitoneal plexuses
R: Retropectoral route
T: Transpectoral route


Axillary lymph nodes
Apical
Central
Lateral
Interpectoral
Posterior
Anterior
Internal mammary lymph nodes

RISK FACTORS FOR BREAST CANCER

NON MODIFIABLE FACTORS:

- Female
- Increasing age
- Early menarche (<12 yrs)
- Late menopause (>55 yrs)
- Nulliparous women
- Family h/o breast cancer
- Genetic (BRCA1 and BRCA2 mutations)
- Previous h/o breast cancer
- Race, ethnics (white women)
- H/o radiation exposure

MODIFIABLE RISK FACTORS:

- Lack of breast feeding
- Age at first live birth (first pregnancy > 30 yrs)
- Parity
- Obese women
- H/o alcohol consumption
- Tobacco intake
- Hormone replacement therapy
- Night works
- Decreased physical activity
- HISTOLOGIC FACTORS:
- Proliferative breast disease
- Atypical ductal hyperplasia
- Atypical lobular hyperplasia
- Lobular carcinoma in situ

BENIGN BREAST DISEASES

Benign lesions are much more common than malignant and about 16% of women of age 40-69 will seek physician regarding breast complaints such as pain, lumpiness or lump.

The diagnosis of a benign breast disease is established withthe use of mammography, ultrasound, and MRI of the breast and biopsieswithout surgery in the majority of patients. Since majority of benign lesions of breast are not allied with a risk for subsequent breast cancer, it is necessary to avoid surgical procedures. It is essential to recognize benign lesions, and also to differentiate in situ and invasive breast cancer. So that we can assess the patient's possibility of developing breast cancer and also provide the mostsuitable treatment.

The term "benign breast diseases" encompasses a heterogeneous group of lesions that may present with the wide range of symptoms. It may be detected as incidental mammographic findings. The incidence of benign breast disease begins to increase during the 2^{nd}decade of life and peaks in the $3^{rd}$and 5^{th}decades, as opposed to the malignant lesions, for which the incidence continues to increase after menopause,but at a less rapid pace.

INFLAMMATORY DISEASES OF BREAST

ACUTE MASTITIS:

Acute mastitis(4) usually occurs in lactating mothers,particularly the first 3 months of postpartum. It is also known as puerperal or lactational mastitis.Most common organism is Staph.aureus. It causes cellulitis of the connective tissue of the breast parenchyma.If left untreated it results in abscess formation and septicemia.

Risk factors are:

- Improper feeding technique
- Cracked or sore nipple and

  Early diagnosis and early management at the stage of cellulitis is necessary to prevent abscess formation. Breast support, local heat, emptying the breast with frequent feeding andexpressing and appropriate antibioticsand analgesics seems to be the most appropriate treatment.

  If antibiotic is given in the presence of abscess it results in ‘antibioma’ formation.

  If infection does not resolve, incision and drainage is usually recommended.Nevertheless, ultrasonogram guided needle aspiration and appropriate antibiotics are better options with excellent cosmetic outcomes.

GRANULOMATOUS MASTITIS(4)

Itmaybe due toinfection, foreign body, or systemic autoimmune disorders. Diagnosis can be made only after microbiological, immunological and histopathological evaluation. granulomatous mastitis is caused by different type of organisms . The most common autoimmune disease are Wegener's granulomatosis and Sarcoidosis.

TUBERCULOUSMASTITIS

Tuberculosis of the breast is a very raremanifestation of TB and often associated with pulmonary tuberculosis /or TB adenitis. However, tuberculous mastitis cannot be diagnosed easily,by clinical and radiological features. It may resemble with either carcinoma of breast or pyogenic abscess of breast. Usually presents with multiple chronic abscesses and fistula.Final diagnosis of the disease is based on bacteriological and histopathological examination.Appropriate anti-tuberculous drug therapy is the treatment of choice.

IDIOPATHIC GRANULOMATOUS MASTITIS

They are granulomatous lesion,for which causeis unkown. The treatment for idiopathic granulomatous mastitis is complete excision of the lesion, followed bysteroid therapy. In 50% of cases even when treated appropriately, persistence, recurrence and complications occurs.The complications are abscess formation, fistulae and chronic suppurative lesions. So long term follow-up is necessary.

FOREIGN BODY REACTIONS

The silicone and paraffin are foreign materialsused for breast reconstructive procedures after mastectomy and also for augmentation. It may cause a foreign body reactions, which is of granulomatous type of reactions in the breast. ‘siliconomas’ are granulomas that occurs afterextracapsular rupture of silicon implant or injection of silicone into the breast. Fibrosis and contractions may develop and forms firm nodules that may be tender.

ZUSKA’S DISEASE: (4)

It is a recurring subareolar abscess that is due to unusual bacterial infection of the breast. It is a triad of:

- cutaneous fistula
- past-like discharge from the nipple and
- H/o multiple recurrentabscesses of the breast.

It is due to squamous metaplasia of the lactiferous ducts, which are obstructed by keratin plugs, causing dilatation of the proximal duct. It then becomes infected and results in abscess formation underneath the nipple and areola. The abscess typically drains at the margin of the areola. Abscess is drainedinitially and after inflammation subsides, complete removal of the duct that is involved and sinus tract excision is done. Butrecurrence of abscess occurs when it involves another duct.

ABERRATION OF NORMAL DEVELOPMENT AND INVOLUTION

This term was described by the Cardiff breast clinic. The principles are:

- Benign breast disorder or disease is due to normal physiological process of reproduction and due to involution
- There is spectrum of conditions that ranges from normal to disease process
- The classification includes pathogenesis and varying degrees of abnormalities

PATHOLOGY:

It includes four features that varies in degree and extent:

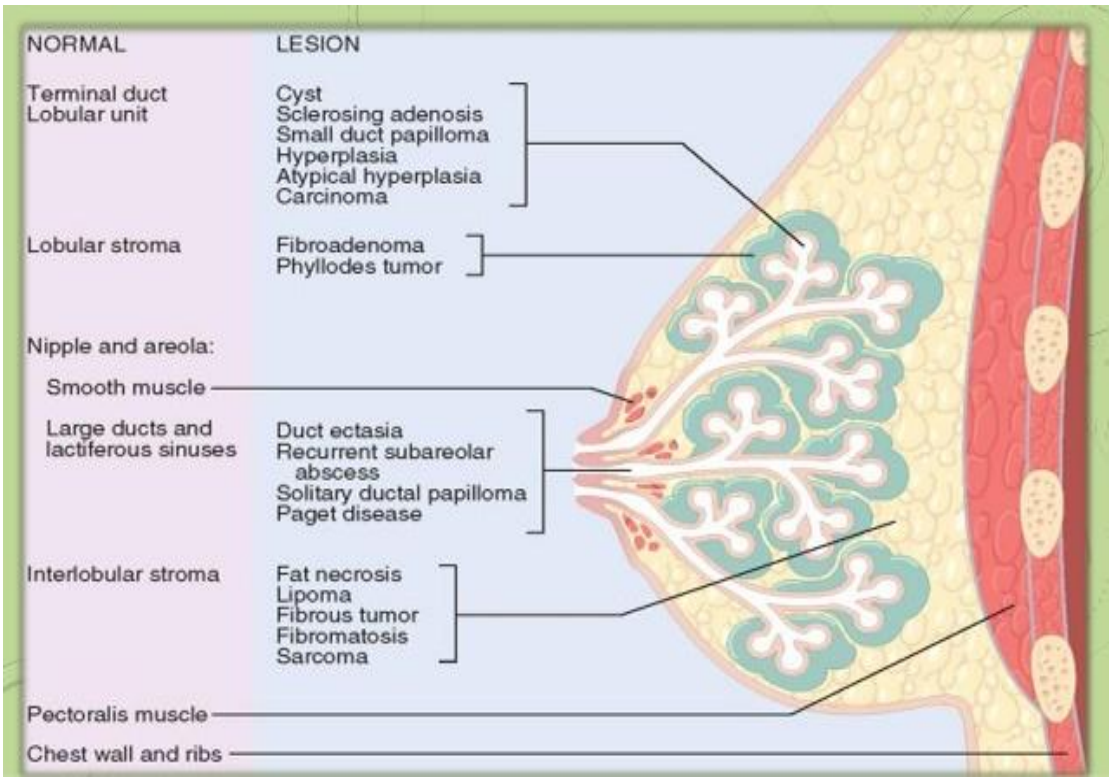
- Cyst formation
- Fibrosis
- Hyperplasia
- Papillomatosis

CLINICAL FEATURES:

Lump – fibroadenoma or cyst

Lumpiness in both breast, may be cyclical and is associated with tenderness.

Non cyclicalmastalgia – in perimenopausal and post menopausalwomen , associated with periductal mastitis or ANDI.



ANDI CLASSIFICATION OF BENIGN BREAST DISORDERS			
	Normal	Disorder	Disease
Early reproductive Years (15-25)	Lobular development	fibroadenoma	Giant fibroadenoma
	Stromal development	Adolescent hypertrophy	Gigantomastia
	Nipple eversion	Nipple inversion	Subareolar abscess
			mammary duct fistula

Later reproductive years (25-40)	Normal	Disorder	Disease
	Cyclical changes of menstruation	Cyclical mastalgia	Incapacitating mastalgia
		nodularity	
	Epithelial hyperplasia of pregnancy	Bloody nipple discharge	
Involution age(35-55)	Lobular involution	macro cyst	
		Sclerosing lesion	
	Duct involution		
	dilatation	Duct ectasia	Periductal mastitis
	sclerosis	Nipple retraction	
	Epithelial turnover	Epithelial hyperplasia	Epithelial hyperplasia with atypia

NON PROLIFERATIVE DISORDERS

They account for 70 % of benign disorders and they do not carry any risk for the development of cancer. It includes:

1) BREAST CYSTS:

Macrocysts are involutionaldisordesand are often multiple.

They are fluid filled, epithelial lined cystic cavities present within breast parenchyma.

Sizes vary from microscopic to large palpable massesand may contain 20 to 30 ml fluid. The fluid can be straw color, dark green or opaque and also contains debris.It can be aspirated ,no further treatment is required. But 50 % of cysts are multiple and recurrent.It is seen in women > 35 yrs of age and it is influenced by ovarian hormones.

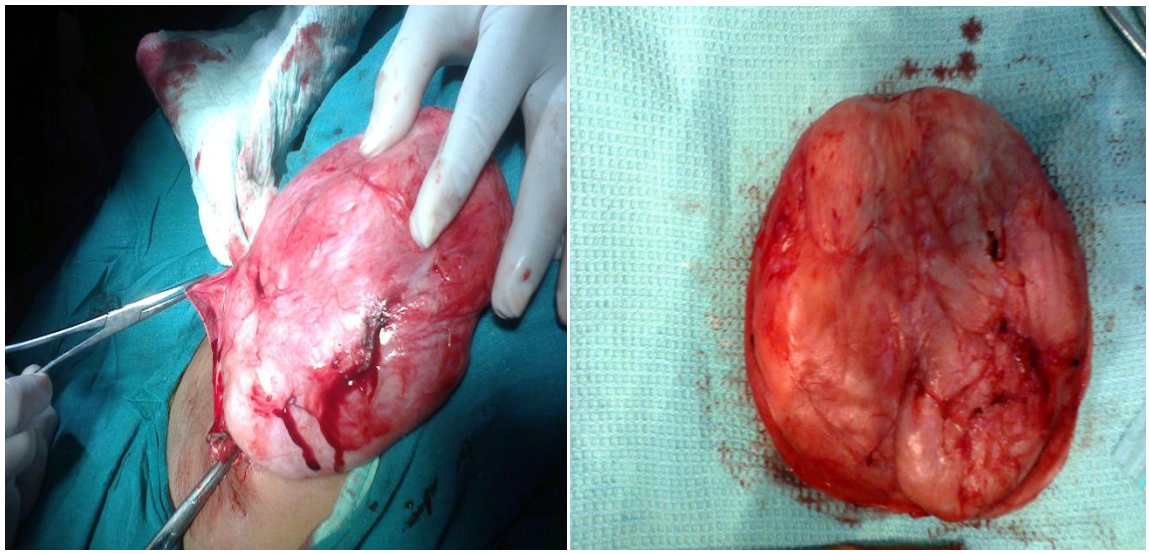
The incidence of intracystic carcinoma is 0.1 %. If there is recurrence after aspiration for 2 times, solid component has to be evaluated by cystopneumography and the aspirate is sent for cytological analysis. The core biopsy or FNAC is done to rule out solid component, cystadenocarcinoma which is common in elderly women.Indications for surgical removal are recurrence after multiple aspirations and dependingupon the needle biopsy report.

2) DUCT ECTASIA:

It is characterized by palpable dilated subareolar ducts which is filled with green or brown secretions,that may present with nipple discharge.This may lead to periductal mastitisor even abscess and fistula. Sometimes presents with indurated mass behind the nipple or slit like nipple retraction mimicking carcinoma. Another theory suggests that periductal inflammation is responsible for ductal dilatation. It can be treated with antibiotics, however excision of all major ducts (Hadfield's operation) is the only option for complete cure.

3) FIBROADENOMAS

It is the 2nd most common tumourof the breast after carcinoma and it is a benign tumour made of epithelial and stromalelements. It is the most common tumour inwomen < 30 yrs of age. They present as a freely mobile, palpable firm mass, referred as breast mouse. They are well encapsulated with the smooth or lobulated surface. The size more than 5cm is termed as Giant fibroadenoma. Development of cancer in fibroadenoma is very rare, of which 50 % are LCIS, 35 % of neoplasia are infiltrating 15 % are intra ductal carcinoma.



GIANT FIBROADENOMA

4) HAMARTOMAS AND ADENOMAS:

Adenomas are composed of benign epithelium packed closely to form a sheet of glands with scanty stromal elements, which distinguishes it from fibroadenoma. They may increase in size during lactation and pregnancy. They are of two types: tubular and lactating adenomas. The tubular variety is seen in young non pregnant women. Lactating adenomas are found during pregnancy and postpartum period.

Hamartomas are discrete,firm well circumscribed tumours measuring 2 to 4 cm in diameter. They contain tightly packed lobules and prominent extralobular ducts.

PROLIFERATIVE BREAST DISORDERS WITHOUT ATYPIA:

1) PAPILLOMASAND PAPILLOMATOSIS:

Papillomas are true polyps of breast duct which are lined by epithelium and are located close to the areola at a peripheral location. It can be solitary or multiple. It is pinkish,friable lesion,attached by stalk to the wall of the involved duct.They are often accompanied by bloody nipple discharge.They present as palpable mass beneath the areola very rarely. The size varies from < 1 cm to 4 or 5cm. It is excised through circumareolar incision. They rarely undergo malignant transformation.

Papillomatosis is referred as epithelial hyperplasia that fills the individual ducts resembling polyp without fibrovascular tissue, associated with fibrocystic changes.It commonly occurs in younger women

2) SCLEROSING ADENOSIS:

It refers to increase in number of terminal aciniassociated with proliferation of stromal tissues. It is indistinguishable both grossly and histologically from carcinoma. The mammogram may show deposition of calcium in a pattern similar to microcalcification found in intraductal carcinoma.

3) RADIAL SCAR:

It is acomplex sclerosing lesion which contains microcysts, epithelial hyperplasia,adenosis and central sclerosis. It mimics carcinoma mammographically with irregular spiculations in the surrounding stroma. In mammogram larger lesions appear as spiculated mass with distortion of architecture and even produce skin dimpling clinically. They have moderate risk to develop into carcinoma. Hence it is necessary to rule out carcinoma by excision biopsy.

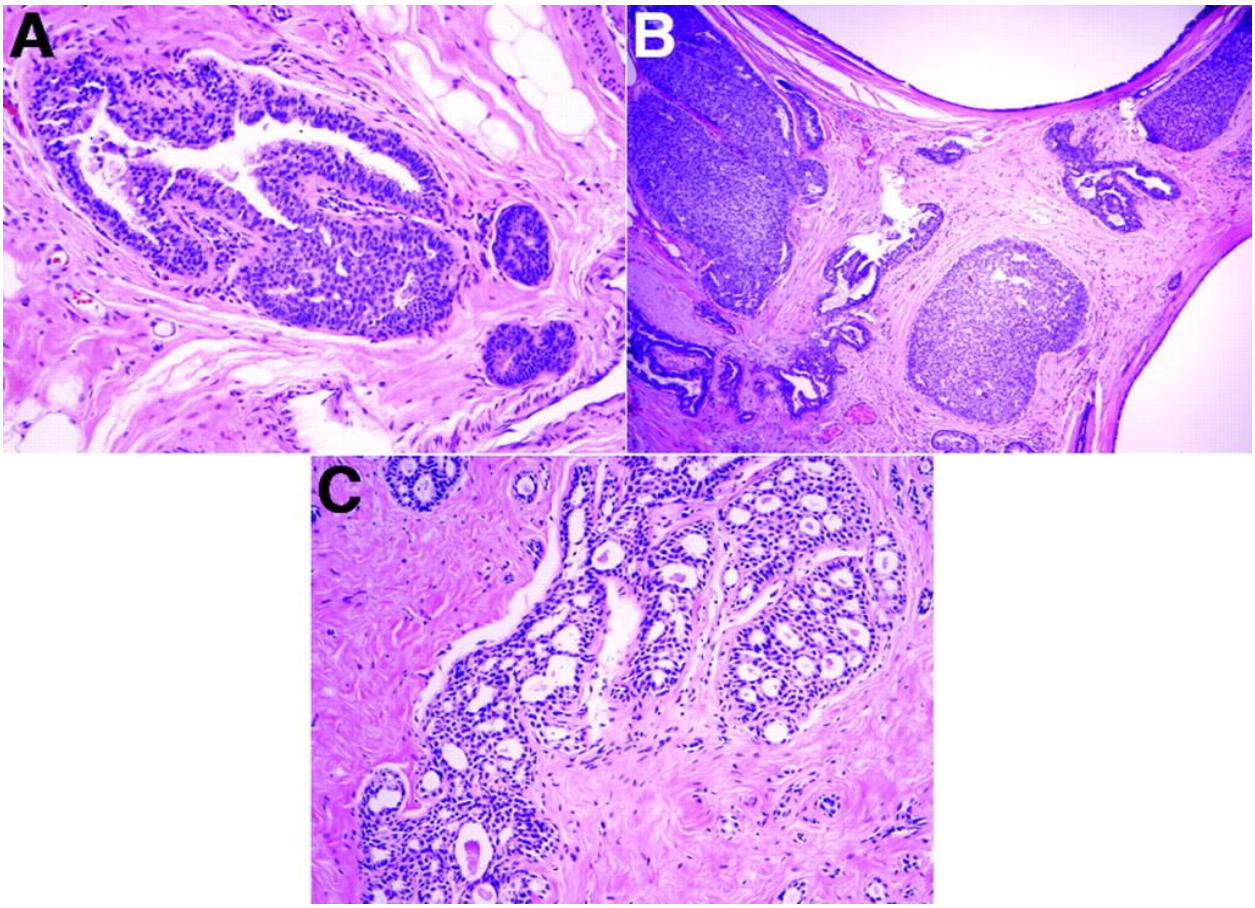
4) DUCTAL HYPERPLASIA:

Mild: Presence of 3 or 4 layers of cells over basement membrane.

Moderate: presence of 5or more layers above the basement membrane.

Florid: epithelial hyperplasia occupying atleast 70 % of minor duct lumen. It carries 1.5 to 2 fold increased risk for cancer.

The most important features of epithelial hyperplasia are an mixture of different cell types :epithelial cells, myoepithelial cells and metaplastic apocrine cells , and variation in the appearances of epithelial cells and their nuclei.



(A): Usual ductal hyperplasia: proliferating epithelial cells that partially occlude the lumen.

(B): Florid epithelial hyperplasia. Proliferating clusters of hyperplastic cells with overlapped and unevenly distributed nuclei. It obliterates and distends the duct lumens.

(C): Atypical ductal hyperplasia: It is characterized by monotonous proliferation of regularly arranged cells(cribriform pattern). Although it displays features of low-grade intraductal carcinoma, this lesion is interpreted as atypical ductal hyperplasia ,as it is seen only in a single and small focus.

ATYPICAL PROLIFERATIVE DISEASES:

Atypical ductal hyperplasia (ADH):

It was described based on exclusion criteria, i.e. the presence of some but not all of the features of DCIS and also lack usual features of epithelial hyperplasia. It mimics low grade DCIS. Lesions less than 2mm in maximum dimension, involving few or a portion of ducts is described as ADH and a larger one as DCIS. It is seen in 4% of symptomatic benign biopsies and 31% of biopsies performed for microcalcifications.Premenopausal women ADH have a higher risk invasive cancer.It requires excision biopsy of the lesion for confirmation,as core needle biopsy cannot establish the diagnosis

Atypical lobular hyperplasia(ALH)

The features of lobular type epithelial proliferations are very similar, and the only difference between ALH and LCIS is the extent and degree of epithelial proliferation, and ALH is characterized by minimal distension of lobular units compared to LCIS made of monomorphic cells with fully distended aciniwhile maintaining the overall lobular architecture.Both the lesions are regarded and managed as a risk factor rather than precursors for invasive cancer.

Both ADH and ALH have4 fold increased risk for cancer development.

CANCER RISK ASSOCIATED WITH BENIGN BREAST DISORDERS AND IN SITU CARCINOMA OF THE BREAST

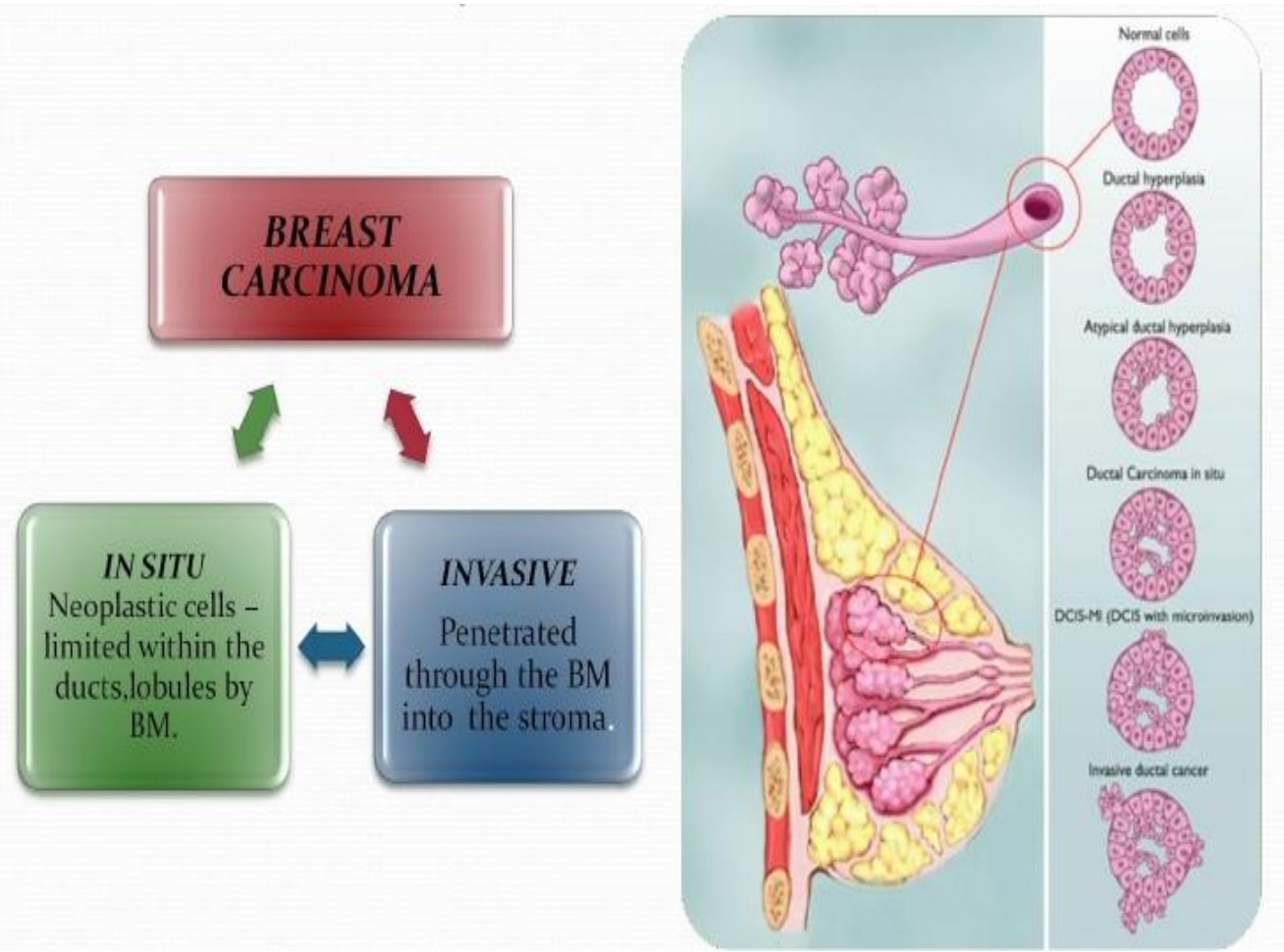
Abnormality	Relative risk
Non proliferative lesions of the breast	No increased risk
Sclerosingadenosis	No increased risk
Intraductal papilloma	No increased risk
Florid hyperplasia	1.5 to 2 fold
Atypical lobular hyperplasia	4 –fold,
Atypical ductal hyperplasia	4 –fold, 10 fold (first degree relative +)
Ductal involvement by cells of atypical ductal hyperplasia	7 -fold
Lobular carcinoma in situ	10 -fold
Ductal carcinoma in situ	10 fold

FAT NECROSIS:

It presents with palpable mass clinically mimicking carcinoma and also produces density which contains calcium on mammogram. It has no malignant potential. It occurs following a surgical procedure,or trauma or radiation treatment.

PATHOLOGY OF BREAST CANCER

The breast cancer arises from the ductal epithelium anywhere from the lactiferous duct to the terminal lobule. With the advent of breast cancer screening, in situ lesions are the more common finding compared to the invasive cancer.



There are three grades of differentiation of tumour:

Well differentiated,moderately differentiated or poorly differentiated.

BLOOM RICHARDSON GRADING OF CARCINOMA BREAST

TUBULE FORMATION:

- **Score 1**: >75% of tumor area forming tubules
- **Score 2**: 10% to 75% of tumor area forming tubules
- **Score 3**: <10% of tumor area forming tubules

NUCLEAR PLEOMORPHISM:

- **Score 1**: Nuclei uniform in shape, relatively small size in comparison with normal breast epithelial cells, uniform nuclear chromatin.
- **Score 2**: nuclei are intermediate size, normal with open vesicular nuclei, visible pleomorphic nucleoli
- **Score 3**: Vesicularrelativelylarge nuclei, with prominent nucleoli, marked variation in size and shape, occasionally with bizarre forms.

MITOTIC COUNT:

- **Score 1**: less than or equal to 10 mitoses per 10 high power fields
- **Score 2**: less than 20 and more than 10 mitoses per 10 high power fields
- **Score 3**: greater than 20 mitoses per 10 high power fields

OVERALL GRADE:

- **Grade 1**: scores of 3, 4, or 5 (LOW)
- **Grade 2**: scores of 6 or 7 (INTERMEDIATE)
- **Grade 3**: scores of 8 or 9 (HIGH)

CLASSIFICATION OF PRIMARY BREAST CANCER(2)

Non invasive epithelial tumours:

- Lobular carcinoma in situ
- uctal carcinoma in situ

Invasive epithelial tumours:

- Invasive ductal carcinoma

1. Not otherwise specified(50- 70%)
2. Special types:
    a. Tubular
    b. Mucinous
    c. Medullary
    d. Colloid
    e. Invasive cribriform
    f. Invasive papillary
    g. Adenoid cystic
    h. Metaplastic

- Invasive lobular carcinoma (10%)
- Mixed Epithelial and connective tumours:
    a. Phylloides
    b. Angiosarcoma
    c. Carcinosarcoma
    d. Adenocarcinoma

CARCINOMA IN SITU:

Broder's described in situ lesions are those in which tumour cells do not invade into the surrounding stroma and are confined to the ductal and alveolar boundaries.With the aid of screening mammography,increased incidence of in situ lesions was demonstrated.

LCIS:

It is developed only in females and characterized by conformity to normal duct lobules and contains distended and filled acini.Multicentricity occurs in 60 -90 % of women and bilateralityoccurs in 50 -70 % of women with LCIS.LCIS is a marker for increased risk of invasive breast cancer.The patients are counseled for screening procedures, chemoprevention and prophylactic bilateral mastectomy.

DCIS:

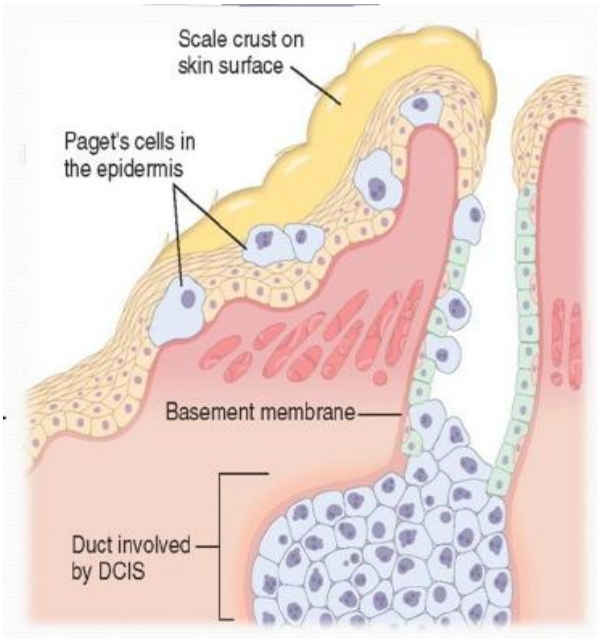
It is characterized by malignant epithelial cells proliferation within the breast parenchymal structures with no evidence of the basement membrane invasion.

Incidence is 5- 10 %, although predominantly occurs in female breast,it accounts for 5% of male breast cancers and is also referred as intraductal carcinoma. There are four morphological categories: papillar, cribriform, solid ,andcomedo.The solid and comedo types of DCIS are higher grade lesions.Its progression to invasive cancer is high(5 fold).It is an anatomic precursor of invasive ductal carcinoma. Microcalcificationsare common features of DCIS.

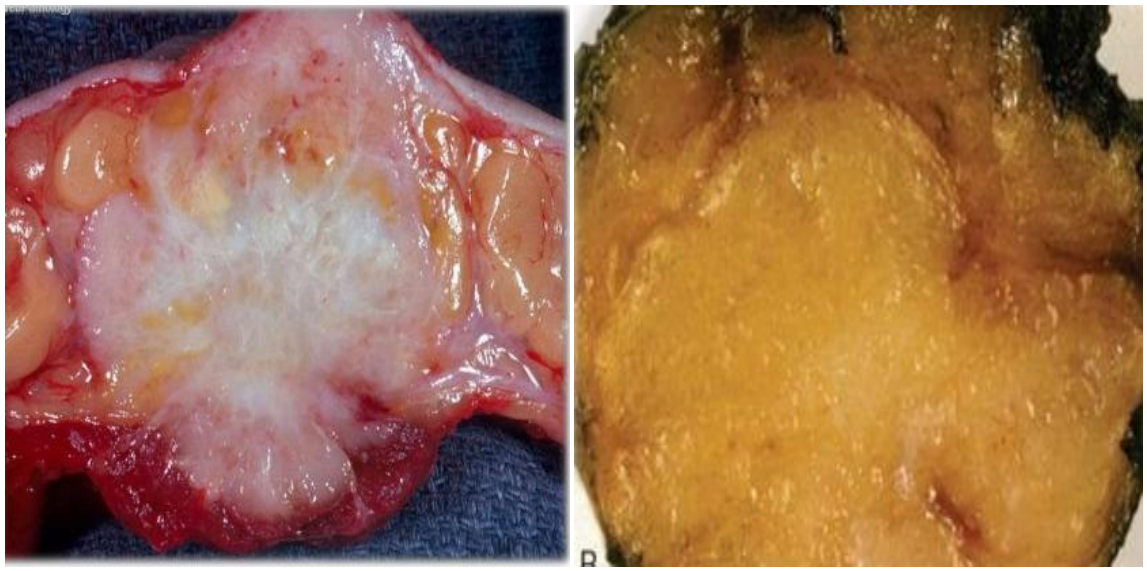
INVASIVE BREAST CARCINOMA:

They are characterized by lack of architecture, variable amount of stromal infiltration and formation of sheets of cells.About 80 % of invasive breast carcinomas are NOS type of invasive ductal carcinoma.

Paget's disease of the nipple presents with eczematous eruption of nipple, mass may or may not be present. Paget's cells/ malignant cells extend from the DCIS lesion along the lactiferous duct to the nipple skin without involving the basement membrane.



Invasive ductal carcinoma is also known as infiltrating ductal carcinoma.When it does not have any special featureit is referred as NST type .It presents with firm,solitary mass in perimenopausal and post menopausal women.60 % of cases presents with axillary lymph node metastasis.

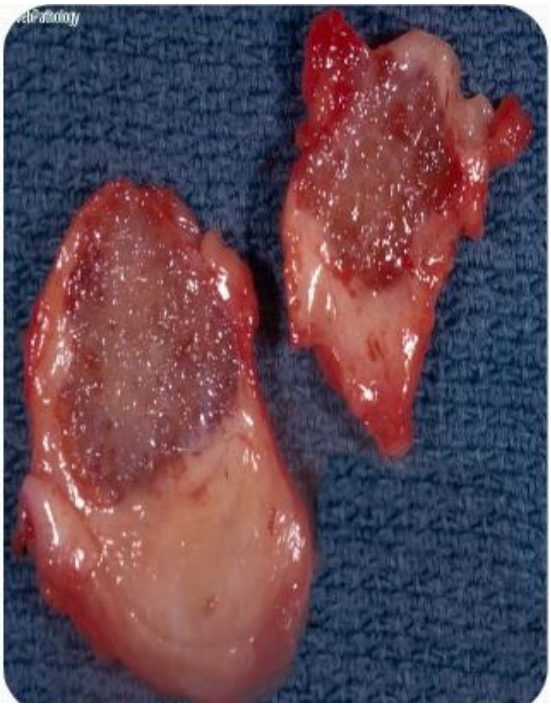


A) Invasive ductal carcinoma B) Medullary carcinoma

Medullary carcinoma accounts for 4% of invasive breast cancers.Bilaterality is seen in 20% of cases and it is a frequent type of BRCA1 breast cancer.These patients have a better survival rate.It is characterized by peculiar invasive cells with increased mitoses and high grade nuclear features.

Medullary variants are high grade, estrogen and progesterone receptor negative and also her2/neu negative. They are termed as triple negative tumours.

Mucinous carcinoma , is a low grade cancer,accounting for 2% of invasive breast cancers.90 % of mucinous tumours show hormone receptors and lymph node metastasis occurs in33% of cases.Because of the presence of mucinous content,cancer cells sometimes are not evident, hence require multiple sections for evaluation to diagnose the tumour.



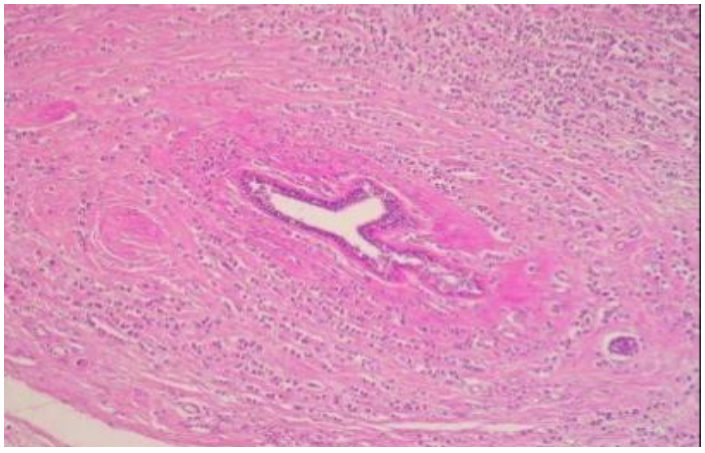
Mucinous carcinoma

Papillary carcinoma presents in seventh decade and accounts for 2% of all invasive cancers. They are characterised by papillae with fibrovascular core and multilayered epithelium.

Tubular carcinomas accounts for 2% of all invasive cancers. It is characterized by infiltrating cells forming glands lined by row epithelium.

Invasive lobular carcinoma accounts for 10% of breast cancer and has features of small lobular neoplastic cells arranged in a single file,giving an Indian file pattern. It is usually multifocal,multicentricand bilateral. It is difficult to detect because of its insidious growth pattern and subtle features in mammography. >90% of lobular cancers are Estrogen receptor positive.

Metastasis occurs to areas such as peritoneum, retroperitoneum, leptomeninges, GIT, ovaries and uterus



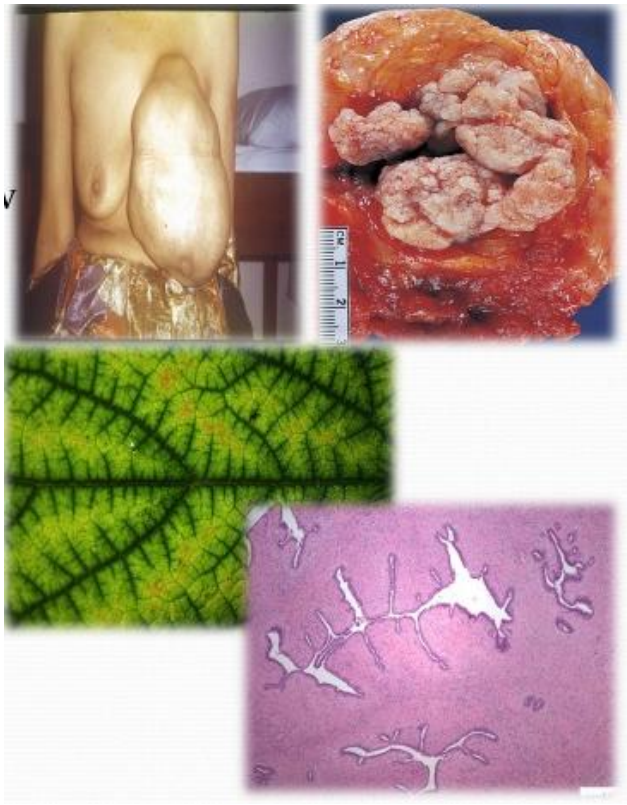
Indian file pattern

OTHER TUMOURS OF BREAST

PHYLLOIDES TUMOUR:

They aretumours of mixed connective tissue and epithelium. They are demarcated from the surrounding ductal elements of breast, which appears compressed and distorted by swirls of fibroblastic growth. They have mixed gelatinous, solid and cystic substances. This gives a classical leaf like appearance (phylloides).

They are classified as benign, borderline and malignant. Benign are tumour masses with average size of 5 cm. They resemble fibroadenoma but the stroma is more cellular. They are indistinguishable mammographicallyfrom fibroadenoma. Hence, Excision biopsy followed by histopathology gives the final diagnosis.



Excision is sufficient for benign tumour.

Borderline tumours are excised with 1cm margins to prevent local recurrence.

Malignant tumours are treated similar to any soft tissue sarcomas. Complete surgical excision of the tumour along with the surrounding normal tissue is the option. When the tumour is very large simple mastectomy can be done.

Metastasis occurs to lungs, bone, abdominal organs and mediastinum hematogeneously.

ANGIOSARCOMA

They are vascular tumours arising from the breast after radiation therapy. It is also seen developed in the upper extremity of post radical mastectomy patients with lymphedema.

TNM STAGING FOR BREAST CANCER

PRIMARY TUMOUR

Tx	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	DCIS,LCIS,Paget's of nipple
T1	Tumour<2cm
T2	Tumour>2and <5cm
T3	Tumour>5cm
T4a T4b T4c T4d	Tumour of any size with chest wall extension Tumour of any size with skin involvement Both T4a and T4b Inflammatory carcinoma

REGIONAL LYMPH NODES

Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis to mobile ipsilateral level1 and 2 axillary nodes
N2a N2b	Metastasis to ipsilateral level 1 and 2 axillary lymph nodes , fixed to one another Metastasis to ipsilateral internal mammary nodes in the absence of level 1 and 2 Axillary LN
N3a N3b N3c	Metastasis to ipsilateral infraclavicular LN with or without level 1 and 2 axillary LN or ipsilateral internal mammary nodes Metastasis to ipsilateral internal mammary and axillary lymph nodes Metastasis to ipsilateral supraclavicular lymph nodes

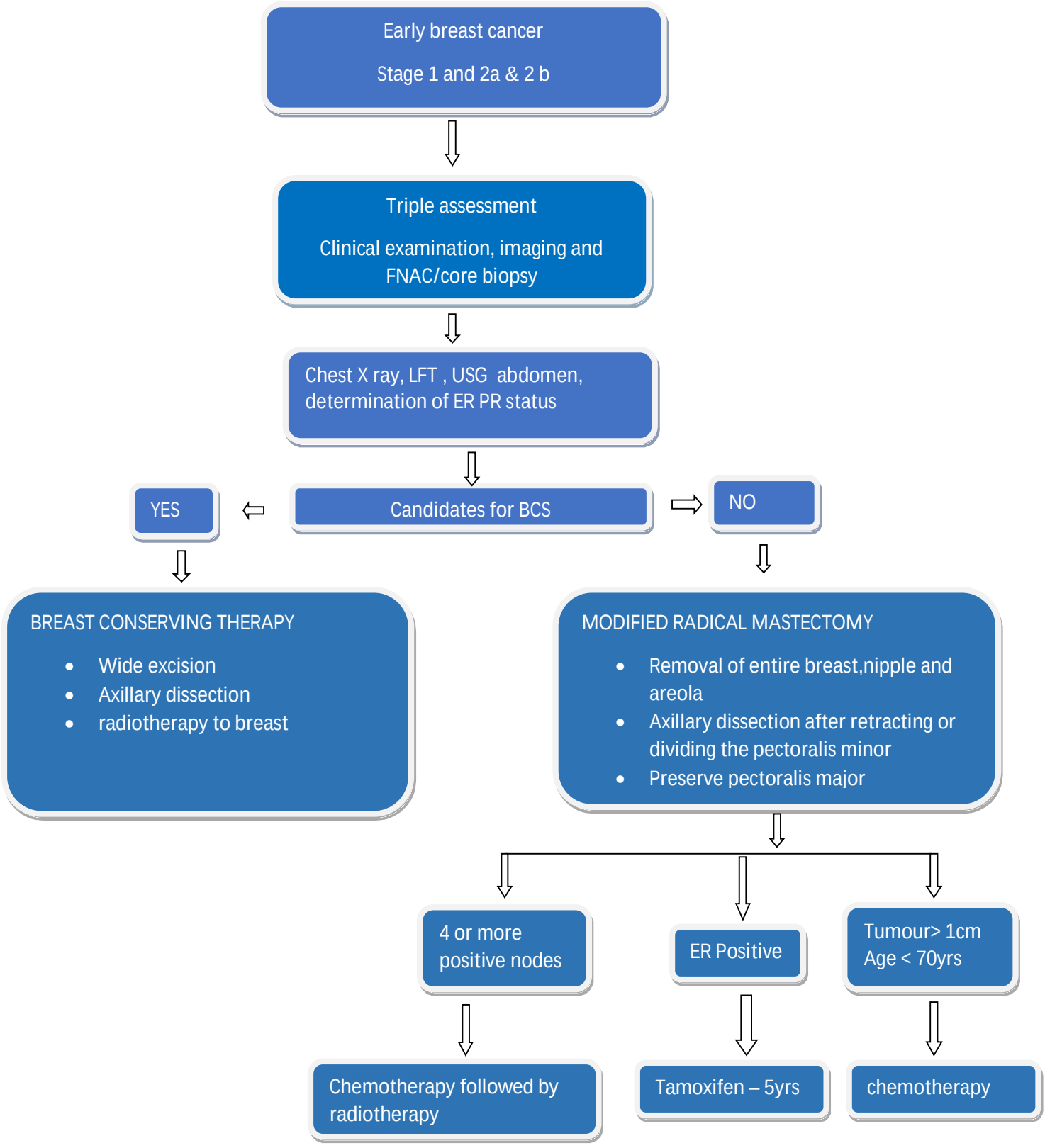
DISTANT METASTASIS

Mx	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

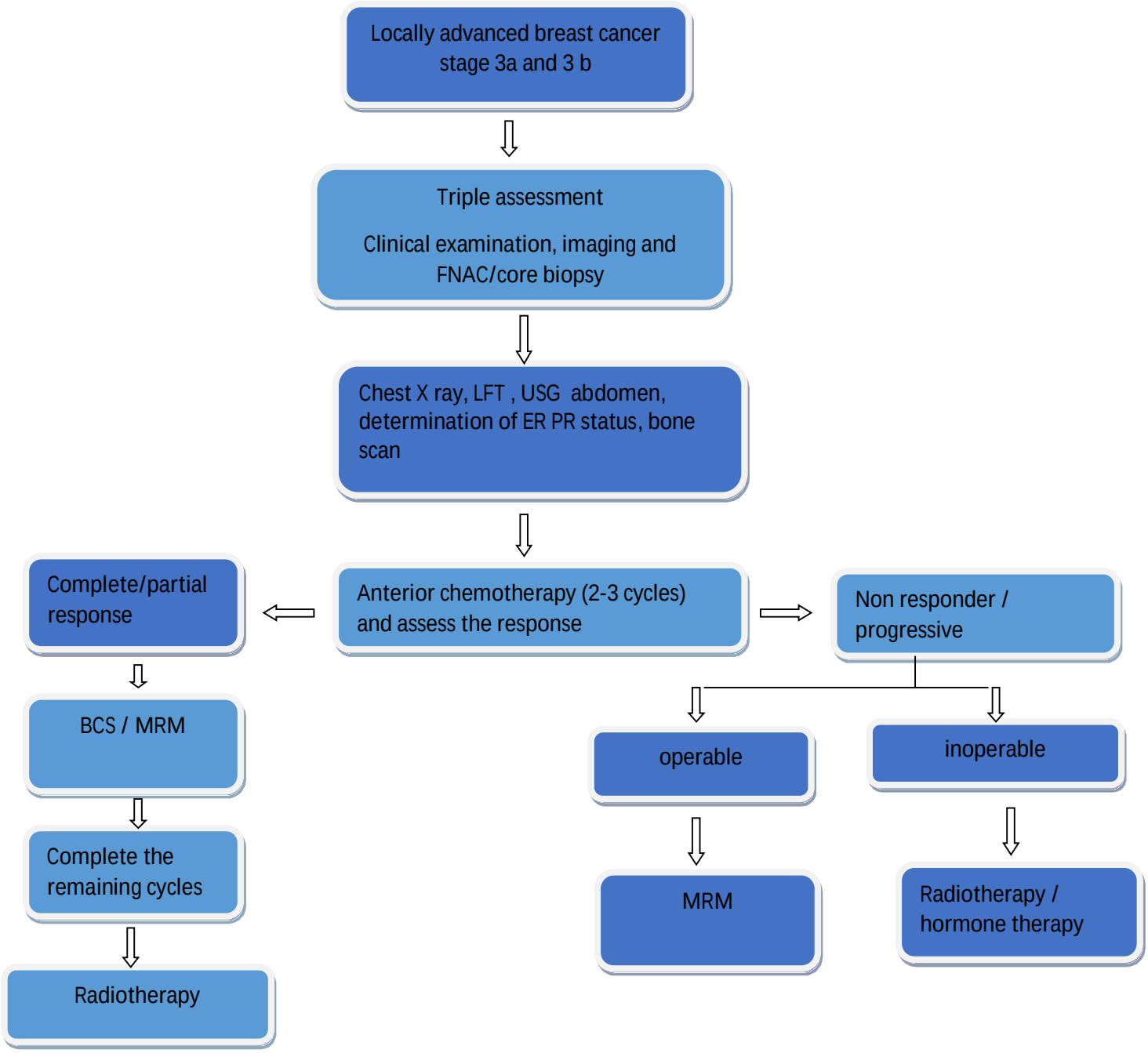
TNM STAGE GROUPINGS

Stage 0	**Tis**	**N0**	**M0**
Stage 1	**T1**	**N0**	**M0**
Stage 2a	**T0**	**N1**	**M0**
	T1	**N1**	**M0**
	T2	**N0**	**M0**
Stage 2b	**T2**	**N1**	**M0**
	T3	**N0**	**M0**
Stage 3a	**T0**	**N2**	**M0**
	T1,T2	**N2**	**M0**
	T3	**N1**	**M0**
	T3	**N2**	**M0**
Stage 3b	**T4**	**N0**	**M0**
	T4	**N1**	**M0**
	T4	**N2**	**M0**
Stage 3c	**Any T**	**N3**	**M0**
Stage 4	**Any T**	**Any N**	**M1**

MANAGEMENT OF EARLY BREAST CANCER



MANAGEMENT OF LOCALLY ADVANCED BREAST CARCINOMA



METASTATIC BREAST CARCINOMA:

Toilet mastectomy, hormone therapy, radiotherapy, chemotherapy and immunotherapy.

INVESTIGATIONS

Triple assessment:

- Clinical examination
- Imaging (mammogram/ultrasound)
- FNAC/core biopsy

MAMMOGRAPHY

Screening mammogramis done in asymptomatic patients with anaim of identifying breast cancer at an early stage. Ithas a better prognosis and it requiresa less aggressive treatment.American cancer society recommends annual screening for women > 40 years of age. Soft tissue radiographs of low voltage and high amperage are taken.The dose is 0.5cGy.The sensitivity and specificity increases with age as breast tissue is replaced by fat.

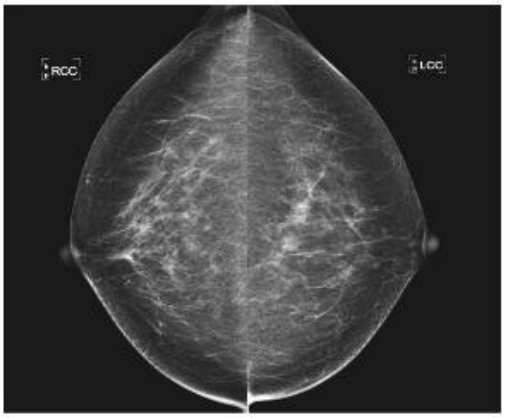
Diagnostic mammography is done to evaluate further in a patients with clinical findings and in patients with abnormalities in screening mammogram.

The primary signs are:

- Spiculated mass
- Clustered pleomorphic microcalcification

The secondary signs are:

- Asymmetrical tissue density
- Skin thickening
- Focal distortion of tissues



Digital mammography is superior to traditional mammography for younger women with dense breast.

Non palpable mammographic abnormalities:

They are clustered microcalcifications and abnormal densities such as architectural distortions and asymmetries that are not palpable clinically. The breast Imaging Reporting and Data System is used to categorizing such lesions which are suspicious.

BREAST IMAGING REPORTING AND DATA SYSTEM (BI –RADS)

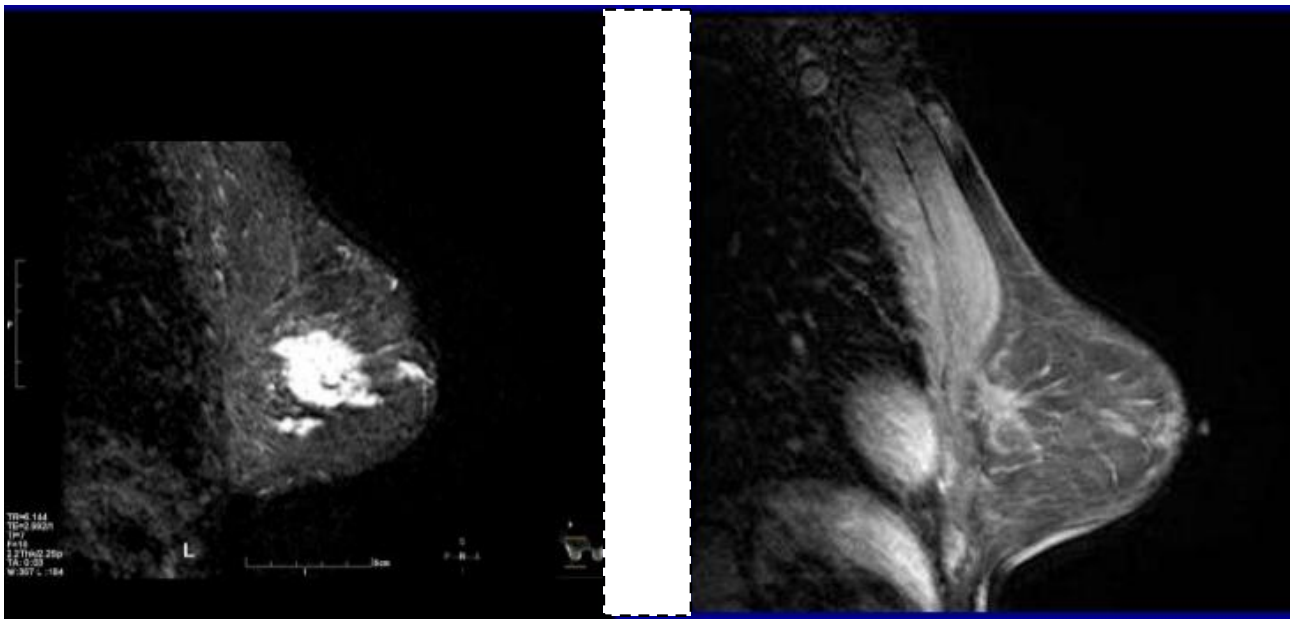
CATEGORY	DEFINITION	REMARKS
0	Incomplete assessment	Need additional imaging, or prior mammogram for comparing.
1	negative	Nothing to remark, recommend annual screening
2	benign	Annual screening
3	Probably benign	Initial short period follow up
4	Suspicious abnormality (2-95%)	Biopsy is required
5	Highly suggestive of malignancy (95%)	Appropriate steps has to be taken
6	Known biopsy	Proven malignancy

ULTRASONOGRAPHY:

It is useful in patients with dense breast and also to determine whether the swelling is solid or cystic. Breast cancer has smooth margins with acoustic enhancement and irregular walls . The combination of ultrasonogram and mammogram increases the diagnostic yield.It is not a good screening tool. It is used for guided FNAC and core needle biopsy.

MAGNETIC RESONANCE IMAGING:

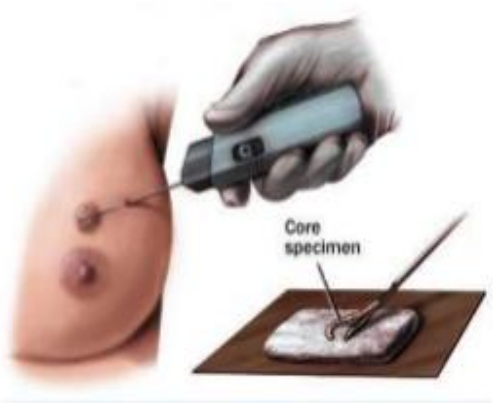
- It is useful to identify the primary lesion in a axillary node positive patient with absent mammographic evidence of the lesion in the breast
- To evaluate the extent of tumour in the dense breast
- To evaluate invasive lobular cancer and to detect contralateral tumour in women with unilateral lesion in mammography
- To distinguish scar from recurrent disease in patient who had undergone BCS
- Gold standard for imaging patients with breast implants
- Screening tool in high risk patients with BRCA mutation
- The sensitivity for invasive tumour is >90% and for DCIS <60%.



MRI breast showing mass lesion before & after neoadjuvant chemotherapy

FNAC:

Done with 22 or 23 G needle with an appropriate syringe and the needle is inserted repeatedly with negative pressure in the syringe.The aspirate is properly smeared on a slide for cytological examination. It is rapid and a least invasive technique. It is accurate if the pathologists and operator are well experienced. False negatives occur due to errors in sampling and it is difficult to distinguish in situ lesions from invasive tumours.



FNAC CORE NEEDLE BIOPSY

CORE NEEDLE BIOPSY:

Procedure of choice for both palpable lesions and also for non palpable image detected lesions. After local anaesthetic infiltration 11gauge core biopsy needle is injected into the lesion with vacuum assistance.<10% patients show inconclusive results. It is difficult to distinguish between ADH and DCIS from invasive lesion in limited sample. The core biopsy showing cellular fibroadenoma may require excision to rule out phylloidestumour. This preoperative distinction of the tumourmay be clinically relevant for: (1) planning the extent of the surgical operation especially if they are considering breast-conserving

surgery; (2) considerations regarding neoadjuvant chemotherapy; and (3) the increased risk of contralateral disease in the case of invasive lobular carcinoma warranting contralateral radiological examination (MRI).

PITFALLS IN FNAC:

- There is difficulty In diagnosing low-grade malignancies and papillary lesions
- It is based on subjective assessment hence there is inevitable difficulties in maintaining consistency and reproducibility in findings
- For large tumours (>4 cm) the accuracy rates are low.
- Calcified lesions are associated with a higher rate of insufficient sampling.
- The diagnosis of tubular carcinoma and invasive lobular carcinoma is very difficult.
- The diagnostic accuracy for papillary lesions is variable but low.
- Differential diagnosis between fibroadenoma and phylloidesby FNAC is challenging due to shortage of universally accepted cytological criteria.
- Benign and normal lesions are often difficult to distinguish with FNAC.
- Pregnancy and lactation are associated with atypical breast changes they are often misinterpreted.

- Samples taken may not berepresentative of the lesion and there may be contamination of samples by tissue adjacent to the target lesion
- Fat necrosis is associated with reactive macrophages which resemble malignant cells
- The incidence of inconclusive diagnoses in FNAC of breast tumour ranges from 4% to18%.
- 45– 87% of aspirates of breast samples classified as‘atypical’ and/or ‘suspicious’ are found to be malignant.
- The most common lesions in the ‘inconclusive’ diagnosis are fibroadenomas and fibrocystic changes. Both lesions occasionally cause cellular atypia that would necessitate histologic evaluation to rule out the possibility of malignancy.

FALSE POSITIVE occurs in:

- Papillary lesion
- Epithelial hyperplasia with nuclear atypia
- Radial scar, complex sclerosing lesion
- Fibroadenoma
- Regenerative epithelial atypia
- Skin adnexal tumours

FALSE NEGATIVE occurs in:

- Tumour with central necrosis
- Small carcinoma next to a dominant benign lesion
- Complex proliferative lesion
- Low grade ductal ca, lobular carcinoma and small cell ductal ca

INTRAOPERATIVE CONSULTATION

As there was the need to confirm the nature of the tumour (benign or malignant) and to take therapeutic decisions accordingly,Frozen section technique was developed.

Margin re-excision is the most common indication for reoperation in patients undergoing BCT.

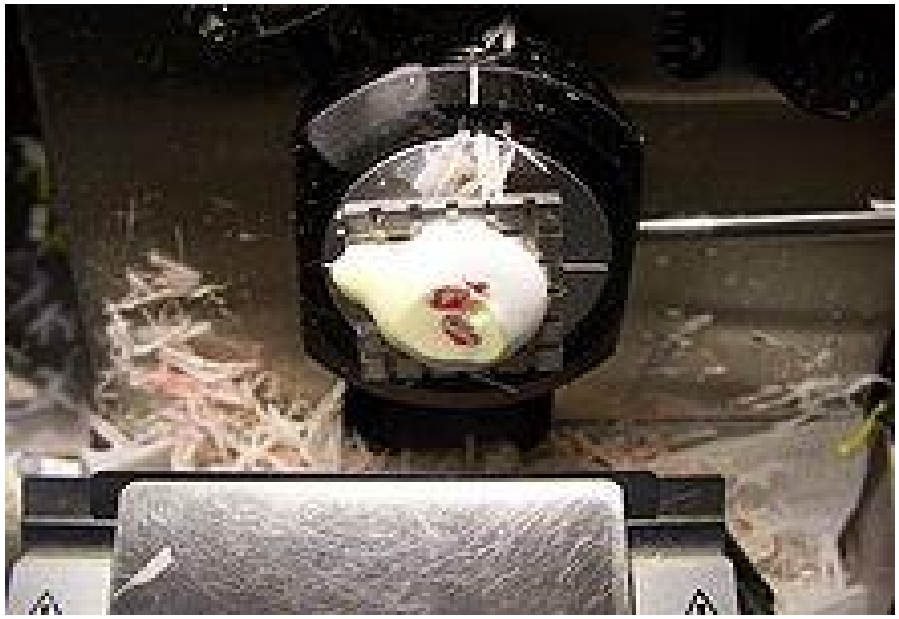
If Patients undergoing breast conservation therapy for early breast carcinomaare given adequate margin and RT they may have similar outcomes comparable to patients undergoing mastectomy.And also inadequate (close) margins have resulted in increased re-excision rate of20% to 70% and re-operation has resulted in increased cost of health care and increased risk of surgery and delay to subsequent radiation and other therapy.

The need for reoperation can be decreased by Intra-operative consultation of sentinel lymph node (SLN) and lumpectomy specimens with the pathologist and resecting the additional breast tissue and/or performing Axillary lymph node dissection during the initial surgery for breast cancer.

FROZEN SECTION

Dr. Louis B Wilson has developed the “FROZEN SECTION” in the year 1905, prior to this, Dr. Thomas S Cullen also was involved in the studies of the same, but only after the fixation with formalin. Then, Dr William Welch, a pathologist experimented with Cullen's procedure but without clinical concerns. Therefore, Dr. Wilson was accredited for pioneering the procedure.

The (5)cryostat is a key instrument used for cryosection, which is principally a microtome inside a freezer. The microtome is capable of slicing sections as thin as 1 micro metre compared to usual histology slice which is cut at 5 to 10 micrometres. The specimen isplaced on a metal tissue disc which is again secured in a chuck .It is then frozen rapidly to about –20 to -30 °C. The specimen is embedded in a gel like medium called OCT. At this temperature, most tissues become rock-hard. The fat or lipid rich tissue usually requires a lower temperature. Each tissue has a preferred temperature for processing. Using microstat portion of cryostat the specimen is cut frozen,and that section is picked up on a glass slide and stained with hematoxylin and eosin. The sample preparation is much more rapid than with traditional histology technique. It takes around 10 minutes compared to 16 hours for histology. However, the quality of the sections is much lower technically.



Tissue embedded within OCT, mounted on a chuck in a cryostat and ready for section production

ADVANTAGES

- If more tissue is needed for making an accurate diagnosis, the surgeon is able to obtain an additional sample, without a second operation.
- If the lumpectomy specimen is found to be cancerous and requires mastectomy the mass can be removed at the same time.
- If the tissue is found to be benign, then it may not require further procedure and thesurgery can end.
- It can help to ensure that the tumourmass and its surrounding borders are removed completely.
- The surgeon and pathologist are able to collaborate to take care of the patient.

LIMITATIONS(5)

The main reason why Frozen section is not routinely done at most institutions are:

- Technical difficulties in freezing tissue.
- It needs costly equipments
- It introduces artifacts due to freezing and
- there is tissue loss during sectioning
- By using standard FS techniques freezing or adequate sectioning of lumpectomy specimens with high adipose tissue isdifficult.
- The Amount of tissue used in frozen section is limited

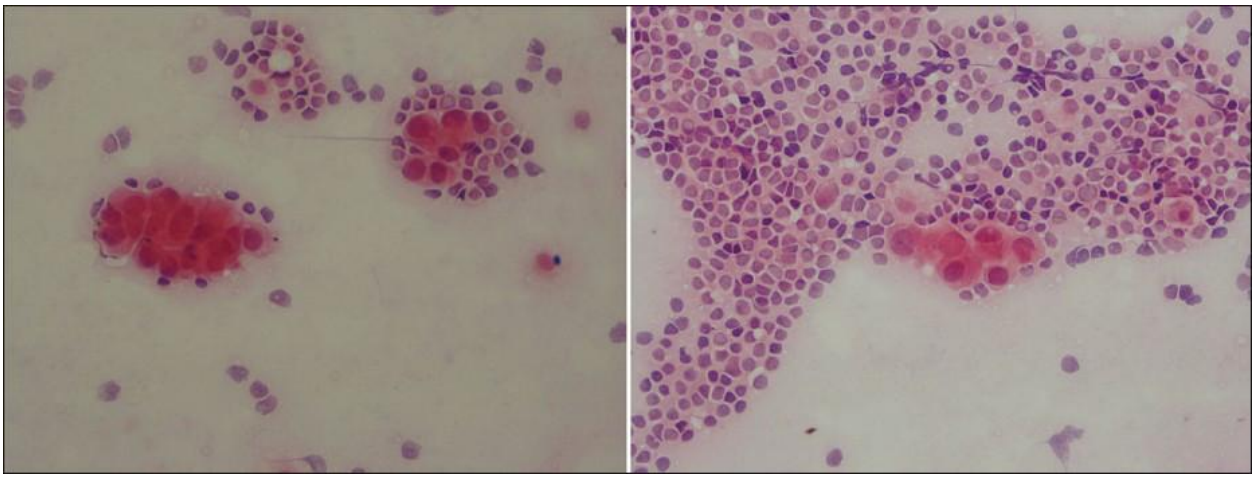
INTRAOPERATIVE IMPRINT SMEAR CYTOLOGY

Imprint cytology (6) is known since 1927. It was first reported by Dudgeon & then by Patrick who did a pioneer work on imprint cytology in conjunction with Dudgeon and in 1934 by Barret. But recently it has achieved recognition as an adjuvant to frozen section for the intra-operative diagnosis.

Suen et al,(7) 1978 observed that for intraoperative diagnosis, intraoperative cytology (imprint smear, scrape smear, touch preparation) canprovide valuable information. It gained popularity and provedto be superior over frozen section.

The imprint cytology became the most common method for analysis as it provided the results rapidly, lacks artefact and was cost effective. It was a benefit for the centers with underdeveloped infrastructure, lack of facilities and lack of trained technicians which was required for frozen section.It may even provide accurate results than frozen section because the entire surface of the resected tumourspecimen is sampled.

The tumour specimen is excised and the imprint is obtained by pressing it onto a glass slide and fixing immediately in alcohol.The smear is stained with haematoxyllin and eosin and it is analysed by pathologist. With experienced handsthe result is obtained within 2 to 15 minutes.



Touch imprint of metastatic ductal carcinoma in a sentinel node

Charles.E.cox(8) and his colleagues first reported evaluation of lumpectomy margins by touch preparation cytology in 1991. He declared that its accuracy was97%.

Andrew J.Creager(9) and his colleagues studied in 141 specimens in 137 patients and concluded that imprint smear is accurate and rapid method for evaluation of margin status.

Study	Year	Sensitivity	Specificity	NPV	NPV	accuracy
Cox	1991	100	96.6	100	88	97.3
Creager	2002	80	85	40	97	85
Saarela(10)	1997	38	85	100	88	-

Mori et al in 2006,(11) conducted a study on intraoperative procedures for assessing sentinel lymph node metastasis in breast cancer. Imprint smear showed sensitivity of 47% andspecificity of 98% and frozen section showedsensitivity of 88% and specificity 100%.

Kennedy (18)reportedsensitivity of 75 to 100% for imprint cytology and 59% to 91% for frozen section.

In 2004 Suzanne klimberg(19) evaluated the use of touch preparation in diagnosis and evaluation of surgical margins and concluded that specificity and sensitivity was 100%.

Valdes EKin 2007,(20)studied the role of Intra-operative touch preparation cytologyin re-excision lumpectomy specimens and reported the sensitivity of 75%, specificity of 82.8%, positive predictive value of 21.4%, and negative predictivevalue of 98.2%.

Sachins.colte in 2010,(21) studied the Role of scrape cytology in intraoperative diagnosis of tumor in 75 cases and 73 could be correctly differentiated into benign and malignant tumors, with an accuracy rate of 97.3%.

François D'Halluin[(22)]studied in 400 lumpectomy cases and concluded that touch preps isreliable and useful method for surgeons in assessing surgical margins in breast conservation surgeries in breast cancer .

The diagnostic accuracy of FNAC was 90.2% and that of imprint 94.1% with no false negatives. Two imprint smears and one aspirate designated suspicious were proved to be benign. The combination of FNAC and imprint cytodiagnosis gave a diagnostic accuracy of 96% thus proving their value in the rapid diagnosis of breast lesions.

Ahamareen,(23) in 2004 assessed and compared the efficacy of Touch Imprint Cytology and frozen section in the diagnosis of various pathological processes. He examined 60 cases who came for intraoperative consultation from various sites of the body.He found that Touch Imprint Cytology alone may provide a correct diagnosis in majority of cases with less expense compared to frozen section that requires sophisticated cryostat machine.

Cherie H.dunphy(24) in 2011, studied Applications of Touch Preparation Cytology in Lymph Nodes and Extranodal Tissues for Evaluation of Hematolymphoid Disorders

Jones L in 2004 (17)concluded that imprint cytology from image guided core biopsy enables the same day diagnosis..

Menes TS in2003(25) studied on intraoperative detection of sentinel lymph node metastases from breast cancer.He reported that touch preparation allowed quick Intraoperative evaluation of the sentinel lymph node metastasis without wasting significant tissue .

Henry S.Tillmanin 2003,studied in 247 patients for 4 Years and reported that touch prep was as accurate as frozen section in detecting lymph node metastasis but it is simple and rapid.

AIM OF THE STUDY

AIM OF THE STUDY

- To evaluate the accuracy of intra-operative imprint smears in breast tumors
- To calculate the sensitivity and specificity of imprint smear in breast tumors
- To correlate imprint smear with histopathological findings

METHODS & MATERIALS

METHODS AND MATERIALS

Study group	**:**	All female patients undergoing elective surgeries for Breast lump
Study design	**:**	Prospective study
Place Of Study	**:**	Department of General surgery, Kilpauk Medical College Hospital Kilpauk, Chennai – 10.
Duration of study	**:**	6 months
METHODOLOGY	**:**	
Inclusion criteria	**:**	Female Patients undergoing elective surgeries for breast
Exclusion criteria	**:**	Patient with acute breast abscess

DATA COLLECTION

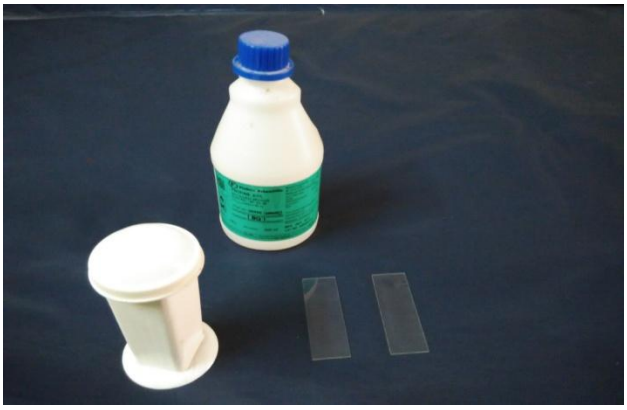
- Clearance from ethical committee obtained.
- Thorough clinical history taken and physical examination were done for all patients.
- Pre-operative investigations done and fitness foranaesthesia and surgery obtained.
- Before surgery, Patient was informed about the procedure and written consent for surgery obtained. Depending upon the FNAC report, each patient underwent surgery either excision biopsy, lumpectomy, simple mastectomy or modified radical mastectomy with or without axillary dissection.

The tumourspecimens before putting into formalin, bisected and macroscopic features inspected. The cut surface of specimenpressed on to a clean non-greasy glass slide after mopping the blood and fixed with isopropyl alcohol. And then, stained with eosin and hematoxyllin. The smears were interpreted by the pathologist.

The imprint smear reports were compared with the final histopathological examination reports.

The results were analysed statistically for sensitivity, specificity and diagnostic accuracy.

MATERIALS USED FOR IMPRINT SMEAR



MICROSCOPIC PICTURES

Fig A
Imprint smear of fibroadenoma showing epithelial and stromal cells

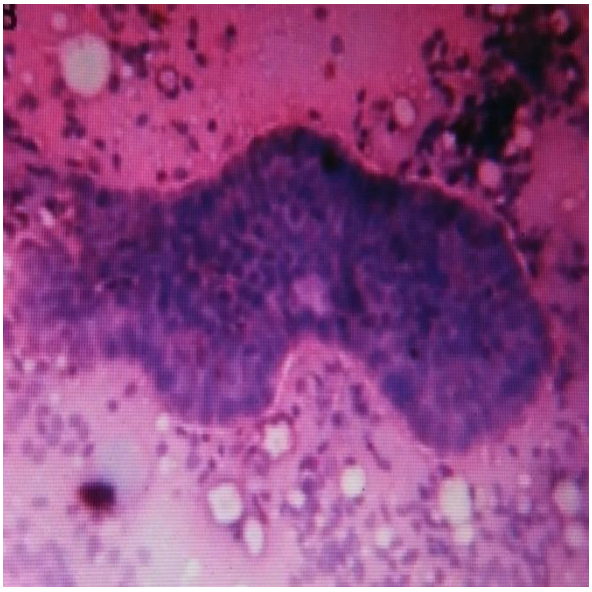


Fig B

hpe of fibroadenoma showing epithelial and stromal cells

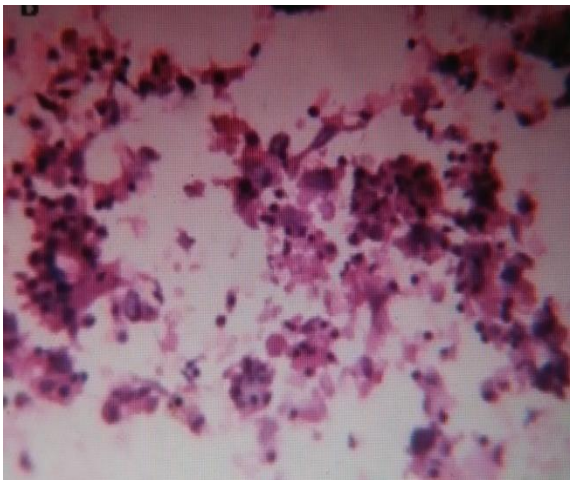


Fig C

Imprint smear of ductal carcinoma showing pleomorphic and hyperchromatic ductal epithelial cells

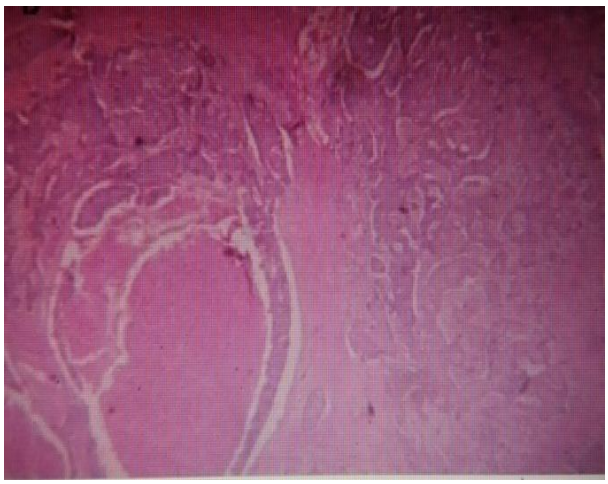


Fig D

Hpe of ductal carcinoma showing comedeo pattern of epithelial cells and neoplastic cells with hyperchromatic and vesicular nuclei

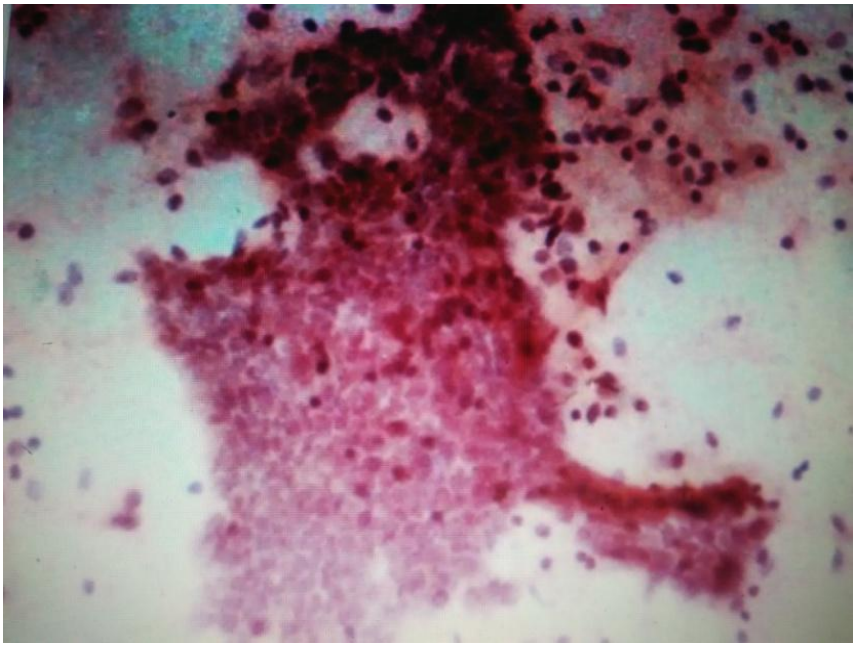


Figure E

Imprint Smear from benign lesion showing uniform arranged ductal cells, with normal nucleus to cytoplasm ratio and fine chromatins

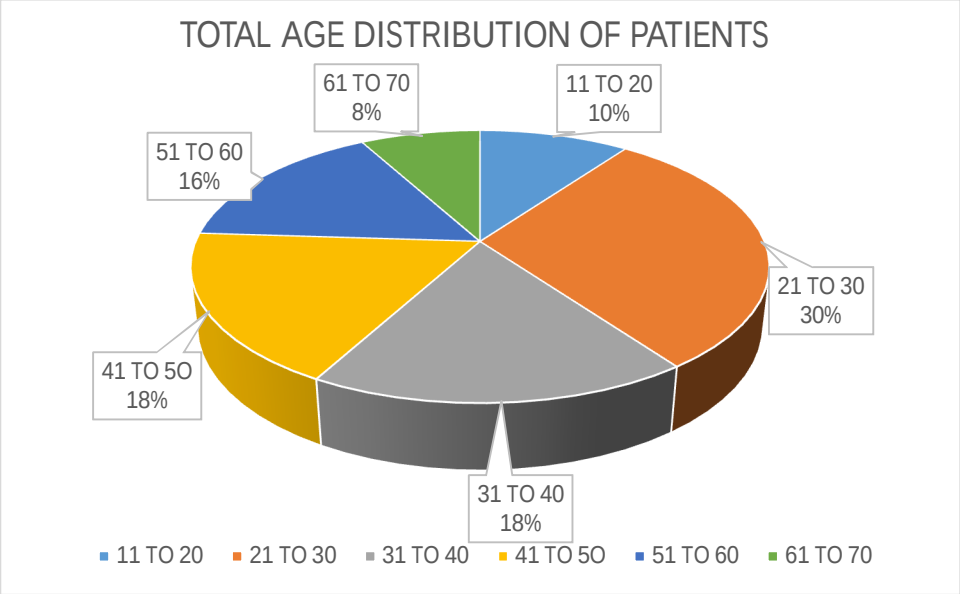
OBSERVATION AND ANALYSIS

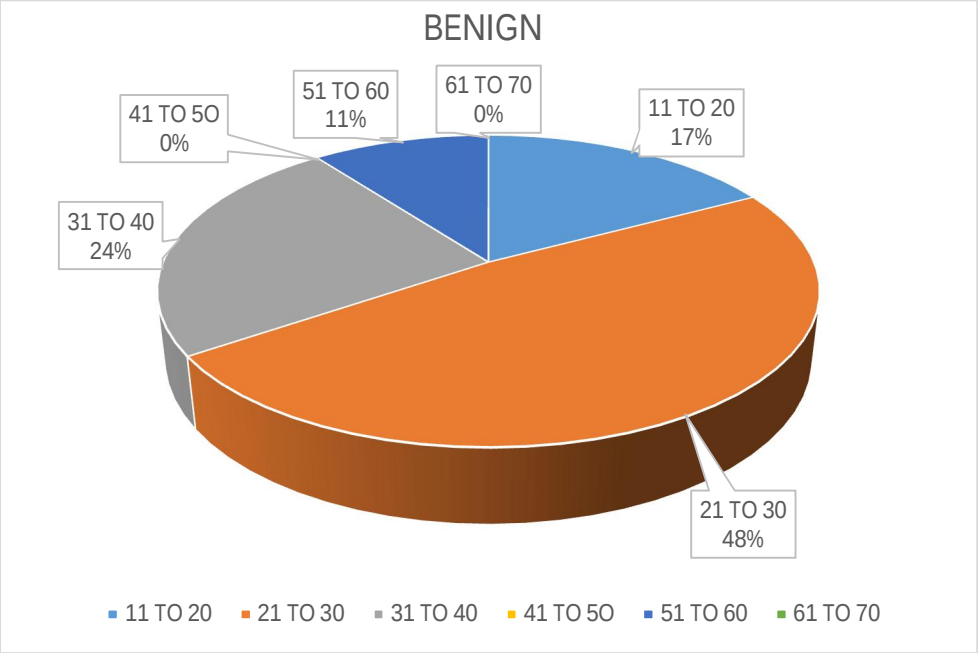
OBSERVATION AND ANALYSIS

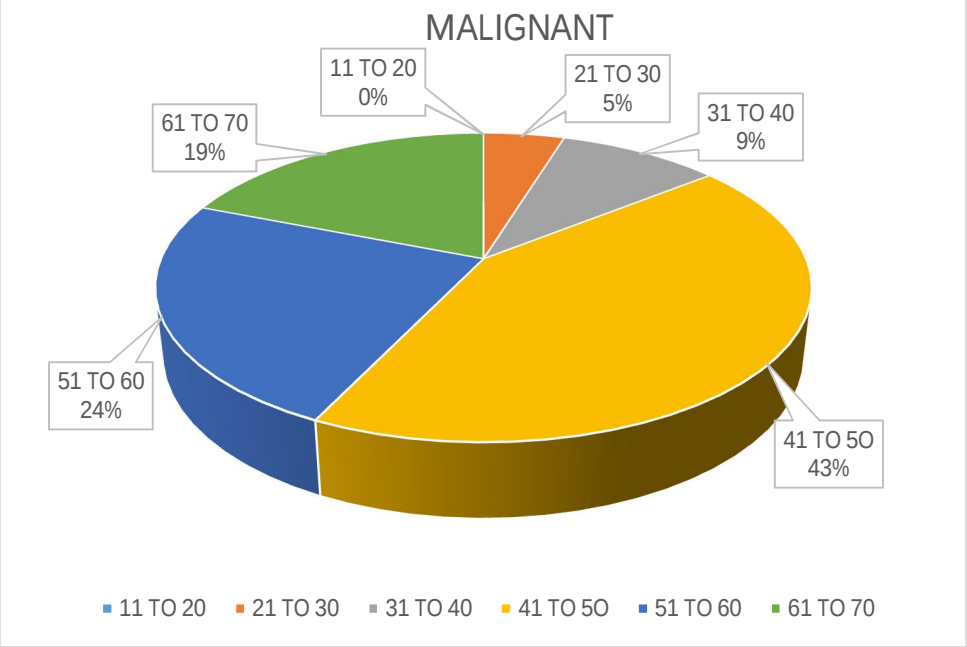
A total of 50 patients who underwent surgeries for breast tumoursbetween2014 to 2015 at our hospital were selected for study as per the inclusion and exclusion criteria.

AGE DISTRIBUTION OF PATIENTS			
AGE OF THE PATIENT	BENIGN	MALIGNANT	TOTAL
11 TO 20	5	0	5
21 TO 30	14	1	15
31 TO 40	7	2	9
41 TO 5O	0	9	9
51 TO 60	3	5	8
61 TO 70	0	4	4

The age incidence ranged from 18 years and 70 years .The benign lesions most commonly involve the age group between21 to 30 years. The malignant lesions commonly involve the age group between 41 to 60 years.




BENIGN
61 TO 70
0%
11 TO 20
17%
51 TO 60
11%
41 TO 5O
0%
31 TO 40
24%
21 TO 30
48%
11 TO 20
21 TO 30
31 TO 40
41 TO 5O
51 TO 60
61 TO 70


MALIGNANT
11 TO 20
0%
21 TO 30
5%
31 TO 40
9%
61 TO 70
19%
51 TO 60
24%
41 TO 5O
43%
11 TO 20
21 TO 30
31 TO 40
41 TO 5O
51 TO 60
61 TO 70

PRESENTATION:

All the patients admitted with the complaints of lump in breast.The other common presentations are pain over the lump/ breast, discharge from the nipple and axillary lump.The duration varied from few months to years.

DURATION OF SYMPTOMS:

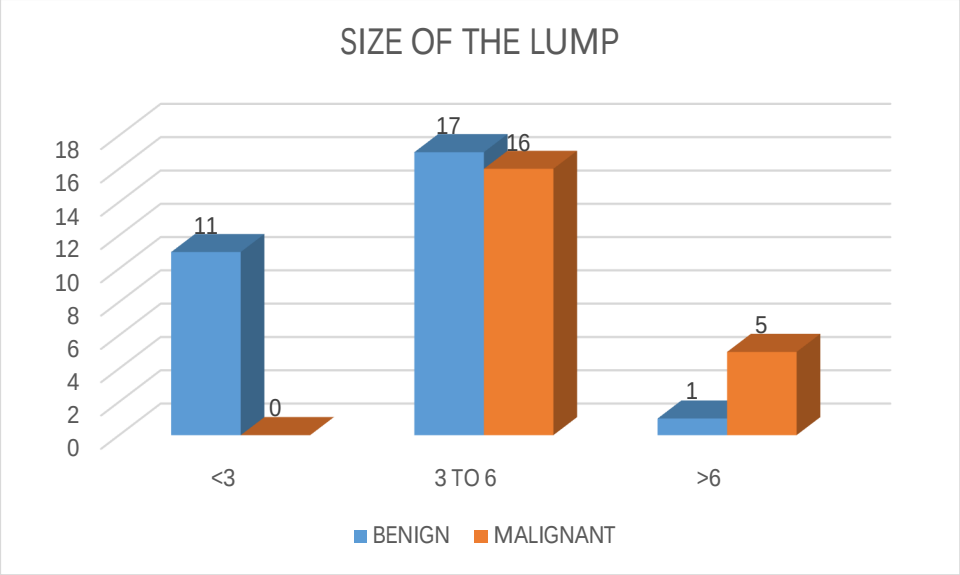
The average duration of symptoms was 5.5 months. The average duration of symptoms for benign tumour was 3.6 months. The average duration of symptoms for malignant tumour was 6.9 months.23 patients had lump in right breast and 27 had lump in left breast.5 patients had lump in both the sides.

Among 50 patients, 2 patients of multiple fibro adenomas had a family history of multiple fibromatosis ,one in mother and other in sister , who also underwent surgeries. 3 carcinoma breast patients had history of ca breast – 2 in mother and 1 in elder sister.

SIZE OF THE TUMOUR:

The size of the tumour varied from 1.5 to 7cm.The size of benign lesions varied from 1.5 to 6cm.The size of malignant lesions varied from 3 to 7cm.

Size of lump	BENIGN	MALIGNANT
<3cm	11	-
3 TO 6cm	17	16
>6cm	1	5
total	29	22



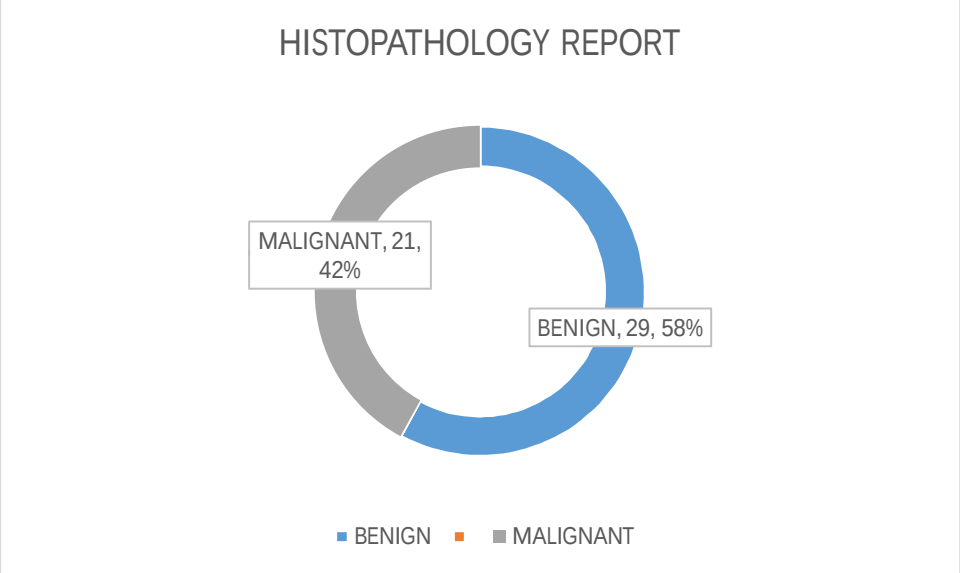
RESULTS OF IMPRINT SMEAR CYTOLOGY

Intra-operative imprint smears are taken from the tumour specimens and correlated with histopathological report.

The imprint smear report showed 30 benign and 20 malignant lesions.

Out of 30 cases, only 1 patient who showed benign lesion in intra-operative imprint smear showed infiltrating ductal carcinoma in histopathological examination, following which she underwent MRM

DIAGNOSIS	NO.OF PATIENTS
BENIGN	30 (false negative -1)
MALIGNANT	20
TOTAL	50

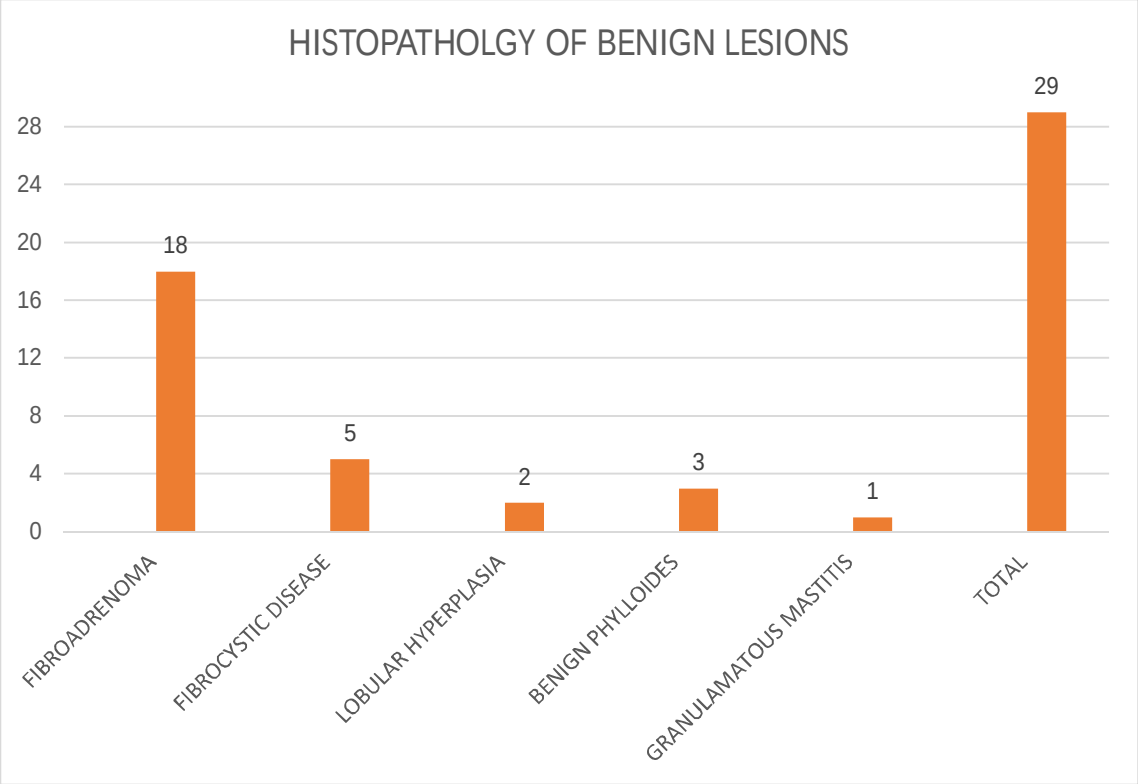


The accuracy rate of the benign tumour is 100%

False positive rate is 0%

HISTOPATHOLOGY REPORT OF BENIGN LESIONS

HISTOPATHOLOGY REPORT	CASES
FIBROADRENOMA	18
FIBROCYSTIC DISEASE	5
LOBULAR HYPERPLASIA	2
BENIGN PHYLLOIDES	3
GRANULAMATOUS MASTITIS	1
TOTAL	29



Out of 20 cases reported as malignant, imprint smear showed 19 cases accurately.

False negative reports may be due to 1) interpretative errors: the morphological changes of the tumour cells particularly in well differentiated ductal and lobular carcinoma that remains subtle and 2) insufficient cells: due to the presence of more fibrous stroma especially in schirrous type of ductal carcinoma , the number of the tumour cells transferred to the slide is minimal and insufficient.

Accuracy rate of malignant lesion is 95.23%

False negative rate is 4.76 %

Test report	malignant	benign
positive	20(a) True positive	0(b) False positive
negative	1(c) False negative	30(d) true negative

True Positive are those patients diagnosed as positive by the test and actually have the disease.

False Positive are those patients diagnosed as positive by the test and actually do not have the disease.

False negative are those patients diagnosed as negative by the test and actually have the disease.

True Negative are those patients who do not have the disease and diagnosed as negative by the test.

1) Sensitivity

It is the ability of the test to identify all the patients who have the disease.

Sensitivity =True positive/ (True positive +False negative)

= a / (a + c) * 100

= 20 / 21 * 100

= 95.23%

2) Specificity

It is the ability of the test to identify correctly all those patients who do not have the disease

Specificity = True negative / (True negative + False positive)

= d / (d + b)* 100

= 30 / (30 + 0) * 100

= 100%

3) Positive predictive value (PPV)

PPV = True positive / (True positive + False positive)

= a / (a + b) * 100

= 20 / 20 * 100

= 100%

4) Negative predictive value

NPV= true negative / (true negative + false negative)

= d / (d + c) * 100

= 30 /31 * 100

= 96.77 %

$$\text{Diagnostic accuracy} = \frac{\text{True positive + true negative}}{\text{True positive +False positive + True negative +False negative}} * 100$$

$$= \frac{20 + 30}{20 + 0 + 30 + 1} * 100$$

= 50/51 *100 = 98.03 %

DISCUSSION

DISCUSSION

The need for intraoperative diagnostic accuracy of the nature of the tumour has lead to the development of imprint smear and frozen section techniques .It is an essential part of the surgeon during the patient's workup for timely and appropriate surgical intervention. If the tumour is found to be malignant, the surgeon can do extensive dissection and lymph node removal in the same sitting without the need for second surgery.

With increasing incidence of breast cancers it is necessary to diagnose the disease rapidly and accuarately. FNAC, Imprint smear and frozen section are the various methods used in various combination for diagnosis with their advantages and limitations.

FNAC is an OPD procedure which is simple,rapid, painless, cost-effective and relatively non-invasive procedure done without any special equipment or preparation .It eliminates the need for open biopsy procedure. Practically, there is no contraindication to FNAC. It can be done in pregnant women, children and high risk patients without any major complication. But it has its own limitations such as inadequate sampling in smaller lesion and deep seated lesions. Most often diagnosis is 'suspicious of malignancy ',but not confirmatory. In such conditions, the surgeon encounters a dilemma to advise appropriate modality of surgery for the patient.

Frozen section is a standard technique for intraoperative evaluation of the tumour. However it has many limitations such as need of costly equipment, sampling error in large specimen, freezing artefacts.

Imprint smear, scrape smear and touch preparation were described in early 20th century by Dudgeon and Patrick and it is widely used in evaluating the margins in breast conservation surgeries and hence gained popularity.

However all these intraoperative diagnostic methods are not equivalent to the final histopathological examination, which is a gold standard.

In our series, the precision of intra operative imprint smear in breast tumours has been evaluated. In accordance to the hypothesis that neoplastic cells adhere to the slide at a greater degree compared to the fat,this method has been proposed. The sensitivity, specificity,positive predictive value, and negative predictive value has been calculated .

In 1991, Cox and his colleagues reported the intraoperative evaluation of breast tumour using touch preparation in the evaluation of margin status. He reported the specificity of 96.6 % andsensitivity of 100 % in his study of 114 patients undergoing surgeries for breast tumours.

Saarela in 1997, reported that imprint smear was 85 % accurate in contrast to the other studies ,who claimed that it was high.

Klimberg in the year 1998 studied in 83 patients and reported 100 % sensitivity, specificity , PPV and NPV .

Several studies have been conducted to compare the accuracy of imprint smear and frozen section. Tribe CR suggested that imprint plays the role inaccurate diagnosis and can be used in places with lack of trained technicians and equipments. Tomohiko Aihara

compared frozen and touch imprint cytology and reported that sensitivity of both was almost equivalent.

D.S Quill(32) studied in 86 lymph node specimens obtained from 13 patients and reported sensitivity of 93 %, specificity of 98 % and PPV of 98 % for imprint cytology. Singh et al (1982)found accuracy rate of 100 %.Khanna et al(13) reported 98 % sensitivity and 100 % specificity ,Quershi et al (2007) suggested that imprint cytology is a reliable and quick method to evaluate intra operatively in appropriate time.

Hiregoudhar et al reported false negative rate of 2.5 %.

Sushma N Ramrej(34) concluded that it is a quick and reliable method ,when taken into consideration the clinical presentation and macroscopic appearance of the tumour specimen, can provide accurate results.

AleksanderNiziolek , (35) 2013 suggested that intra operative evaluation of sentinel lymph node gives the possibility to proceed with lymph node dissection in one –step and start earlier adjuvant therapy.

In our series, we reported aspecificity of 100 %,sensitivity of 95.23 %, PPV of 100 % and NPV of 96.77 % .Only one case reported as benign found to be infiltrating ductal carcinoma on histopathological examination.21cases were malignant and found to be infiltrating ductal carcinoma. 29cases were benign of which 18 werefibroadenomas , 5 fibrocystic disease, 1 granulomatous mastitis , 3phylloides and 2 werelobular hyperplasia.

In order to avoid re-operation, proper preoperative counselling, triple assessment and intra operative imprint smear is necessary.

As breast conservation surgeries for early breast carcinoma is gaining more importance, intra- operative imprint smear has become a key tool for assessing the status of the tumour margins. Re exicision can be perfomed at the same sitting if the margins are found to be positive, with avoidance of re operation. Many studies has suggested that the risk of local recurrence can be reduced by excising adequate margin around the tumour, giving post-operative adjuvant radiotherapy and using tamoxifen for patients with ER positive tumour.

Intra operative imprint smears are also used in the evaluation of nature of sentinel lymph node.SLN is the node that receives lymphatic drainage first from the tumour site. If sentinel lymph node is positive for tumour,axilla also has to be treated .This is achieved by dissection of level 1 and 2 axillary lymph nodes.

Many researches are in the progress in studying DNA markers and immunohistochemistry in imprint cytology smear. Imprint cytology is gaining importance in also tumours involving cervix, uterus, parotid, thyroid, parathyroid,skin,kidney and prostate and also lymphoproliferative disorders.

With increasing incidence of cancers, the need for early, rapid diagnosis and treatment has developed.Due to limitations of FNAC,in situations wherethe results aresuspicious, open biopsy is done in all centers where there is no facilities for frozen section.

Intra operative imprint smear do not need specialized equipment. It is very rapid, simple and economic diagnostic method for intra operative consultation with accuracy rate similar to frozen section and can be used in the institutions with inadequate surgical pathological laboratory to give an opinion on the nature of tumor.

CONCLUSION

CONCLUSION

Intra operative imprint smear aids in the diagnosis of the nature of the tumour on-table similar to frozen section but at a rapid time using simpler techniques and instruments with the help of cytopathologist. It is also used in determining the status of the margins in breast conservation surgeries and the status of sentinel lymph nodes. This helps the surgeon to take decision on table regarding the surgical procedure to be done without the need for re operation.

Intraoperative cytology has higher accuracy rates. It preserves the cellular details, and there is possibility to identify the focal and macroscopically unidentifiable neoplastic lesion in large tissue fragments.

The disadvantages of intraoperative cytology are very few. With the experience of pathologists higher accuracy rates can be achieved. Though it is not possible to distinguish *in situ* from infiltrating carcinoma and also evaluation of invasion depth, it can be used as an adjunct for histopathological examination.

In the present study, the specificity was 100 %, sensitivity was 95.23 % and overall diagnostic accuracy was 98.03 %.

Finally we concluded that imprint cytology is simple, fast, easy, cost effective and reliable technique for the evaluation of breast tumor intra operatively where the facilities for frozen section is not available. The sensitivity and specificity supports their utility for intra operative diagnosis.

SUMMARY

SUMMARY

To evaluate the accuracy of intra operative imprint smear cytology a study was carried out in 50 patients admitted in our hospital as per inclusion and exclusion criteria. Imprint smears were taken intra operatively and were compared with the histopathological examination.

The results obtained are:

Sensitivity of the test was 95.23 % and specificity was 100 %.

The overall diagnostic accuracy was 98.03 %.

The positive predictive value was 100 % and negative predictive value was 96.77 %.

The accuracy rate for benign lesions was 100 % and for malignant lesions was95.23 %

False positivity 0 %

False negativity 4.76 %

Whenever FNAC reports are inconclusive, intra operative imprint smear aids in the diagnosis of the nature of the tumour and avoids repeat surgeries .it also helps in making decisions in breast conservation surgeries in evaluation of tumour margins .It aids in taking decisions regarding axillary node dissection in the same sitting by assessing the sentinel lymph node status.Recently immunohistochemistry and DNA markers are also being evaluated intra operatively in imprint smears.

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PROFORMA

PROFORMA

NAME: **UNIT NO.:**

I.P.NO.:

AGE/SEX:

OCCUPATION: **DATE OF ADMISSION:**

ADDRESS: **DATE OF DISCHARGE:**

CONTACT NO:

COMPLAINTS:

Lump in breast since duration

Pain in breast since duration

Nipple discharge in breast since duration

Nipple retraction in breast since duration

HISTORY:

PAST HISTORY:

FAMILY HISTORY:

PERSONAL HISTORY:

MENSTRUAL HISTORY:

OBSTETRIC HISTORY:

TREATMENT HISTORY(DRUGS):

GENERAL PHYSICAL EXAMINATION:

HT: **WT:** **BMI:**

VITALS:

BP: **PR:** **RR:**

Breast examination:

INSPECTION:

Arms by the side of the body

Arms raised above the head

Arms pressing the hips

Bending forward

1.Breast:

Position

Size and shape

Puckering or dimpling

2.Skin over breast:

Colour and texture

Engorged veins

Peau`d orange

Dimpling,puckering

Nodules

Ulceration ,fungation

3.nipple:

Presence

Position

Number

Size and shape

surface

Discharge

4.areola:

Colour

Surface

Size and Texture

5.arm and thorax:

Edema

Nodules

6.axilla and supraclavicular fossa

PALPATION

In sitting position

In semi recumbent position

In recumbent position

- Local temperature and tenderness
- Position of lump
- Number
- Size and shape
- Surface
- margin
- consistency
- fixity to breast tissue

- fixity to skin
- fixity to fascia and muscles
- palpation of nipple

EXAMINATION OF LYMPH NODES;

Axillary:

- pectoral
- brachial
- subscapular
- central
- apical

Cervical:

supraclavicular

SYSTEMIC EXAMINATION:

CVS:

RS:

P/A: including PV and PR

CLINICAL IMPRESSION:

INVESTIGATIONS:

RENAL PROFILE

Random sugar	Urea	Creatinine

Complete Hemogram

TC	DC	ESR	HB	Platelet count

ECG all leads

CXR

Fnac

USG breast

Mammogram

USG abdomen

INTRAOPERATIVE IMPRINT REPORT

SURGERY PERFORMED

HISTOPATHOLOGY REPORT

SUMMARY:

CONSENT

நோயாளியன் ஒப்புதல் படிவம்

ஆராய்ச்சியின் விபரம்:.

ஆராய்ச்சி மையம்: அரசு கீழ்பாக்கம் மருத்துவக் கல்லூரி மருத்துவமனை

நோயாளியின் பெயர்: நோயாளியின் வயது:

பதிவு எண்:

நோயாளி கீழ்கண்டவற்றுள் கட்டங்களை (✓)செய்யவும்

1. மேற்குறிப்பிட்டுள்ள ஆராய்ச்சியின் நோக்கத்தையும் பயனையும் முழுவதுமாக புரிந்து கொண்டேன். மேலும் எனது அனைத்து சந்தேகங்களையும் கேட்டு அதற்கான விளக்கங்களையும் தெளிவுபடுத்தி கொண்டேன். ☐

2. மேலும் இந்த ஆராய்ச்சிக்கு எனது சொந்த விருபத்தின் பெயரில் பங்கேற்கிறேன் என்றும், மேலும் எந்த நேரத்திலும் எவ்வித முன்னறிவிப்பின்றியும் இந்த ஆராய்சியிலிலுந்து விலக முழுமையான உரிமையுள்ளதையும், இதற்கு எவ்வித சட்ட பினைப்பும் இல்லை என்பதையும் அறிவேன். ☐

3. ஆராய்ச்சியாளரோ, ஆராய்ச்சி உதவியாளரோ, ஆராய்ச்சி உபயத்தாரோ, ஆராய்ச்சி பேராசிரியரோ, ஒழுங்குநெறி செயற்குழு உறுப்பினர்களோ எப்போது வேண்டுமானாலும் எனது அனுமதியின்றி எனது உள்நோயாளி பதிவுகளை இந்த ஆராய்ச்சிக்காகவோ அல்லது எதிர்கால பிற ஆராய்ச்சிக்காகவோ பயன்படுத்திக் கொள்ளலாம் என்றும் மேலும் இந்த நிபந்தனை, நான் இவ்வராய்ச்சியிலிருந்து விலகினாலும் தகும் என்றும் ஒப்புக் கொள்கிறேன். ஆயினும் எனது அடையாளம் சம்பந்தப்பட்ட எந்த பதிவுகளும் (சட்டபூர்வமான தேவைகள் தவிர) வெளியிடப்படமாட்டாது என்ற உறுதிமொழியின் பெயரில் இந்த ஆராய்ச்சியிலிருந்து கிடைக்கப்பெறும் முடிவுகளை வெளியிட மறுப்புத் தெரிவிக்கமாட்டேன் என்று உறுதியளிக்கிறேன். ☐

4. இந்த ஆராய்ச்சிக்காக என்னுடைய மார்பகத்திலிருந்து அறுவைச்சிகிச்சையின் போது எடுக்கப்படும் கட்டி, புதுமுறையான சதைப் பரிசோதனைக்கு அனுப்பப்படும் என்றும் மருத்துவர் மூலம் அறிந்துகொண்டேன். ☐

5. இந்த ஆராய்ச்சிக்கு நான் முழுமனதுடன் சம்மதிக்கிறேன் என்றும் மேலும் ஆராய்ச்சிக் குழுவினர் எனக்கு அளிக்கும் அறிவுரைகளை தவறாது பின்பற்றுவேன் என்றும் உறுதியளிக்கிறேன். ☐

6. இந்த ஆராய்ச்சிக்கு தேவைப்படும் அனைத்து மருத்துவப் பரிசோதனைகளுக்கும் ஒத்துழைப்புத்தருவேன் என்றும் உறுதியளிக்கிறேன். ☐

7. இந்த ஆராய்ச்சிக்கு யாருடைய வற்புறுத்தலும் இன்றி எனது சொந்த விருப்பத்தின் பெயரிலும் சுய அறிவுடனும் முழு மனதுடனும் சம்மதிக்கிறேன் என்று இதன் மூலம் ஒப்புக்கொள்கிறேன். ☐

நோயாளியின் கையொப்பம் பெருவிரல் கைரேகை

இடம்: தேதி:

ஆராய்ச்சியாளரின் கையொப்பம்

இடம்: தேதி:

MASTER CHART

MASTER CHART

s.no.	IP.NO	Name	Age	Duration of symptoms	Lump size	Breast side	Family history	FNAC	Procedure	Imprint smear	HPE	Remarks
1	6670	SELVA RANI	50	2m	4	R	-	S	TB+MRM	M	IDC	
2	6798	SAROJA	70	6m	5	L	-	S	TB+MRM	M	IDC	
3	6784	SANGEETHA	15	4m	2	R	-	B	EB	B	FA	
4	7854	AMUDHA	22	10m	3	R	-	B	EB	B	FA	
5	7965	PREETHI	18	6m	2	L	-	B	EB	B	FCD	
6	7976	MANJULA	56	5m	4	L	-	S	TB+MRM	M	IDC	
7	8800	RAJESWARI	20	12m	2.5	R	-	B	EB	B	FA	
8	8865	GOMATHI	40	.5m	4	L	-	B	EB	B	IDC	FALSE NEG
9	8976	ANNALAKSHMI	20	2m	3	B/L	-	B	EB	B	FA	
10	8876	JEEVA	55	1m	6	L	-	M	MRM	M	IDC	
11	8978	MALATHI	30	18m	3+2	B/L	PRESENT	B	EB	B	FCD	
12	9123	FARITHA	42	2m	5	R	-	S	TB+MRM	M	IDC	
13	9345	GOMATHI	30	3m	4	R	-	B	EB	B	FA	
14	9321	SANGEETHA	30	8m	2	L	-	B	EB	B	FA	
15	9356	MATHEENA	38	4m	2.5	L	-	B	EB	B	FA	
16	9432	FATHIMA	30	1.5m	2	R	-	B	EB	B	FA	
17	9443	MANGALAKSHMI	35	4m	2	R	-	B	EB	B	GM	
18	9449	JAYANTHI	22	3m	2	R	-	B	EB	B	LH	
19	9564	YAMUNA	24	2.5m	3	L	-	B	EB	B	FCD	
20	9568	INDRA	53	14m	5	L	PRESENT	M	MRM	M	IDC	
21	9588	KAMALA	70	1m	6	L	-	S	TB+MRM	M	IDC	
22	9590	JAYALAKSHMI	37	5m	7	L	-	B	EB	B	PHY-B	
23	9780	PALANIYAMMAL	52	2m	4	L	-	S	EB+MRM	M	IDC	
24	9796	INDRA	53	12m	5	L	-	S	TB+MRM	M	IDC	
25	9998	PRIYA	21	3m	4/1.5	B/L	-	B	EB	B	FCD	
26	11123	LAKSHMI	32	2m	2/1.5	B/L	-	B	EB	B	FA	
27	11234	ARPUTHAMARY	48	4m	5.5	L	-	M	MRM	M	IDC	
28	11243	VALLI	40	5m	5	L	-	B	SM	B	PHY-B	
29	12345	MANJULA	28	1.5m	3	R	-	B	EB	B	FA	
30	12324	SEETHA	35	4m	2/2.5	B/L	-	B	EB	B	FA	
31	13465	SASIKALA	22	6m	3.5	L	-	B	EB	B	FA	
32	13654	KUMARI	50	2m	4	R	--	M	MRM	M	IDC	
33	13876	CHELLAMMA	55	4m	4	R	-	B	EB	B	FCD	
34	13986	RANI	50	2m	6	L	-	S	TB+MRM	M	IDC	
35	13997	BACKIA	44	11m	4	R	-	S	TB+MRM	M	IDC	
36	11465	SAVITHRI	41	3.5m	3	L	PRESENT	M	MRM	M	IDC	
37	14765	BHARATHI	20	10m	3	L	-	B	EB	B	FA	
38	14567	MALINI	35	1m	3	R	-	B	EB	B	FA	
39	14666	SHANTHI	55	4m	3.5	R	-	B	EB	B	FA	
40	14578	MEENA	22	2m	3	L	-	B	EB	B	FA	
41	15676	GAYATHRI	22	1m	3	L	-	B	EB	B	LH	
42	16782	MUTHULAKSHMI	39	1m	2.5	L	-	B	EB	B	FA	
43	17689	MALLIGA	48	.5m	4	L	PRESENT	S	TB+MRM	M	IDC	
44	18432	MANIMEGALAI	33	3.5m	4.5	L	-	S	TB+MRM	M	IDC	
45	18445	SRIDEVI	24	11m	4	R	-	S	TB+MRM	M	IDC	
46	18867	KANNIYAMMAL	66	1.5m	6	R	-	M	MRM	M	IDC	
47	19013	RATHIKA	23	2m	3	R	-	B	EB	B	FA	
48	19024	SUPAMMAL	70	2m	5	L	-	M	MRM	M	IDC	
49	19876	KAMACHI	34	5m	4	L	--	B	EB	B	PHY-B	
50	19998	BAKKIYA	44	4m	6	L	--	S	TB+MRM	M	IDC	

KEYS TO MASTER CHART

B	–	Benign
M	–	Malignant
S	–	Suspicious
EB	–	Excision Biopsy
TB	–	Trucut Biopsy
MRM	–	Modified Radical mastectomy
IDC	–	Infiltrating ductal carcinoma
FA	–	Fibroadenoma
FCD	–	Fibrocystic disease
LH	–	Lobular hyperplasia
GM	–	Granulomatous mastitis
Phy-B	–	Benign Phylloidestumour
B/L	–	Bilateral breast
R	–	Right breast
L	–	Left breast